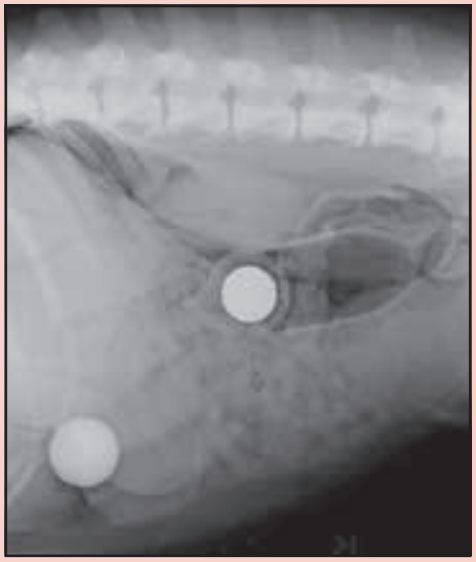
BSAVA
BRITISH SMALL ANIMAL VETERINARY ASSOCIATION

BSAVA Manual of
Canine and Feline
Emergency and Critical Care

third edition







Edited by
Lesley G. King and Amanda Boag

BSAVA Manual of Canine and Feline Emergency and Critical Care

third edition

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Foreword

It is a great pleasure to write the foreword for this third edition of the *BSAVA Manual of Canine and Feline Emergency and Critical Care*. The author list, a literal 'who's who' of international experts in emergency and critical care medicine, was compiled (and individually cajoled, no doubt) by Amanda Boag and Lesley King, two of the most astonishingly accomplished members of the worldwide veterinary critical care community I know or knew. Amanda continues to influence her discipline, and the profession, as a champion of structured training programmes in emergency and critical care and as a champion of 'professionalism' through the RCVS. Sadly, Lesley was taken from us all too soon, in May 2016, mid-way through production of this Manual.

I had the good fortune to work alongside Lesley during my 10 years at the University of Pennsylvania, coincidentally where I also first met Amanda. When I arrived at 'Penn' as a temporary lecturer in surgery in 1991, 4 years qualified and with two RCVS certificates tucked under my arm, I considered myself a high achiever. On my first day, I was introduced to Lesley, who was qualified 1 year longer than me, 'double boarded' (Internal Medicine and Emergency and Critical Care Medicine) and already 'Head' of ICU – the first dedicated veterinary ICU in the world – as well as an established expert in pulmonary medicine. Reality check! I realised my rudimentary knowledge of emergency and critical care, derived almost entirely from the handbook Trauma Management in the Dog and Cat by John Houlton and Polly Taylor, was going to fall short of the mark (with all due respect to Polly and John). I openly confessed to Lesley that I was particularly deficient in this area and that I would need help and so, Lesley added me to her list of 'projects' and through a combination of active and passive mentorship, Lesley and her colleagues, taught me (and many others, including Amanda) about critical care, contextualised to our animal patients. Although Lesley had many attributes that could make her intimidating – she was physically very tall as well as being an intellectual giant – to me, she never was. Lesley could, however, make it quite clear that she didn't agree with my treatment plan by simply peering over the top of her glasses, smiling and saying "I don't think that would be ideal" and then quoting four publications that proved her point!

Both Amanda and I carried this enthusiasm for emergency and critical care back to the UK when we returned, as did others, many of whom are also contributors to this Manual. I have been privileged, largely as a bystander, to witness the emergency and critical care revolution ripple through the UK and Europe at the hands of these advocates, with Dez Hughes and Amanda deserving special mention in this regard. This enhanced understanding of both Emergency Medicine and Critical Care Medicine has saved many lives and improved the quality of the lives of so many patients entrusted into veterinary care. The third edition of this Manual, ultimately made possible because of Amanda's dedication, is a 'must have' for anyone involved in emergency and critical care medicine and represents a massive contribution to animal health and welfare. The Manual is a truly fitting tribute to the global influence of the 'pioneers of emergency and critical care medicine' which included, as a most prominent member, Professor Lesley King.

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Preface

It is a great pleasure to present the newest edition of the *BSAVA Manual of Canine and Feline Emergency and Critical Care*. The specialty of Emergency and Critical Care (ECC) continues to develop rapidly and this book has been thoroughly updated, including many new images, with several new authors joining the team. The chapters outlining the approach to patients presenting with cardiac and neurological emergencies have been rewritten to include current thinking on the best approach to these patients in the emergency setting, and all chapters have been updated to reflect developments on point-of-care ultrasound and colloid fluid therapy. Importantly, we have updated the section on teamwork and expanded on the importance of communication and leadership skills that must go hand in hand with our clinical skills if we are to do the best by our patients.

This Manual is intended as a quick and easy reference for practitioners who handle emergency and critical cases on a routine or even a not-so-routine basis. We hope that the material is accessible and practical, even in a crisis! It also provides a depth of coverage suitable for those studying for their certificate or in the early stages of a residency programme.

As I write this, I am all too aware that I am doing so in the absence of my co-editor Lesley King who very sadly lost her life to cancer in May 2016. Lesley had a huge and lasting impact on our specialty and many of the authors, including myself, benefited enormously from her support, encouragement and wisdom. She is missed by all of us in the ECC community, but her work and influence on our specialty shines through the pages of this Manual.

I would like to express my sincere gratitude to each of the contributing authors. These contributors are truly leaders in their fields both nationally and internationally. Without their efforts it would not have been possible to put together this Manual, which spans the breadth of our knowledge in this vast field. I would also like to acknowledge the incredible contributions of everyone in the BSAVA Office, who all worked tirelessly to make this Manual as perfect as it can be!

Finally, I would like to acknowledge the help and support that I have received from family and friends throughout the process – their encouragement and support is priceless.

I hope that this Manual proves to be useful, helps you to save some lives, and sparks or fuels your interest in the exciting and dynamic field of emergency and critical care.

Amanda Boag
February 2018

and on behalf and in memory of Lesley G. King.

Chapter 1

Triage of the emergency patient

Andrew J. Brown and Kenneth J. Drobatz

Triage can be defined as the evaluation and allocation of treatment to patients according to a system of priorities designed to maximize the number of survivors.

All stages of emergency evaluation are important to the successful management of the critically ill patient: telephone triage; waiting room triage; primary survey and initial treatment; and secondary survey and the emergency plan. Critically ill patients have little physiological reserve to tolerate mistakes of omission or commission. Anticipation and prevention of problems before they occur is one of the cornerstones of optimal emergency and critical care medicine. Always assume the worst and treat for it, while maintaining the philosophy: 'above all, do no harm.'

Telephone triage

The initial contact between a client and the veterinary surgery or hospital is often via the telephone. The information obtained from this conversation may assist in triage of the patient, may help in diagnosis, and may provide information regarding first aid treatment for the pet.

The immediate aim of telephone triage is to determine whether the patient needs to be examined by a veterinary surgeon (veterinarian) immediately and what the owner should do for the pet before coming to the surgery. The owner should be calmed if necessary, so that concise and accurate information can be obtained. Questions should determine:

- The level of consciousness
- How the animal is breathing
- The colour of the mucous membranes
- The nature of the injury
- The presence and severity of bleeding
- The presence and severity of wounds
- The ability of the animal to ambulate
- The presence of obvious fractures
- The severity of vomiting and diarrhoea if present
- The presence of urine and the ability to urinate
- The degree of abdominal distension
- Whether there is coughing.

Patients where the owner reports any of the following should be brought to the hospital without delay:

- Collapse
- Respiratory distress
- Severe coughing
- Neurological abnormalities
- Protracted vomiting
- Slow or rapid heart rate
- Bleeding from body orifices
- Weakness, pale mucous membranes
- Rapid and progressive abdominal distension
- Inability to urinate
- Toxin ingestion
- Extreme pain.

Transport and preparation

Owners often want to administer first aid to their pets, but it is often better to encourage them to bring the animal to the clinic as quickly as possible. When the problem is clearly determined and relatively simple, advice can be given over the telephone. However, relying on an owner's interpretation of the animal's problems can be risky. If there is any doubt about what is occurring, the owner should be advised to bring the pet to the clinic for definitive evaluation.

If trauma has occurred, steps should be taken to protect the spine. The animal should be lifted gently on to a rigid board or blanket, and transported by carrying the improvised stretcher rather than the animal itself. Fractured limbs can sometimes be stabilized for transport by wrapping a roll of newspaper around the limb or taping or tying a board or piece of cardboard to the leg. The joints above and below the fracture should be stabilized. Splints should be applied with care, since it is often difficult for the owner to determine the location of the fracture. If done incorrectly, splinting has the potential to cause further damage. If doubt exists, the animal should be placed in a confined space or in an area where movement is minimized. Direct pressure or careful application of a tourniquet can control active haemorrhage. Owners should be warned that animals that are in pain, traumatized, neurologically damaged or frightened should be approached carefully and muzzled if possible. Even the friendliest of pets can become aggressive under these circumstances.

Clients may be extremely upset and should be calmed prior to transporting their pet. Clear directions should be given to the owner for the drive to the clinic, and time of arrival should be estimated. The hospital personnel should be notified about the nature of the emergency and the estimated time of arrival, so that any special preparations may be undertaken.

Triage and initial assessment

Triage is the sorting out and classification of patients to determine priority of need and the optimal order in which they should be treated. Upon arrival at the veterinary clinic, every animal should be evaluated promptly and rapidly by a trained member of the medical team to determine whether it requires immediate treatment or is stable enough to wait if necessary (Figure 1.1). During the triage, a brief (30 second) history is obtained about the nature of the primary complaint and its progression. Animals that are in containers or blankets should be taken out and examined. Four major organ systems should be assessed:

- Respiratory
- Cardiovascular
- Neurological
- Renal.



1.1 Following triage evaluation, unstable patients are taken to the treatment area for initial assessment.

Dysfunction in any one of these systems can become life-threatening and should be addressed as rapidly as possible.

Respiratory rate, rhythm and effort should be determined. Signs of respiratory distress include loud airway sounds, increased breathing rate, abducted elbows, extended head and neck, flaring of the nares, open-mouth breathing, cyanosis and paradoxical respiration (see Chapter 7).

Cardiovascular system assessment includes mucous membrane colour, capillary refill time, and pulse rate, quality and rhythm. Signs of cardiovascular compromise include pale, grey or hyperaemic mucous membranes, very rapid or prolonged capillary refill time, weak or bounding pulse, very rapid or slow pulse rate and an irregular or asynchronous pulse rhythm (see Chapter 3).

Immediate neurological assessment should include evaluation of mentation and ability to ambulate. Neurological abnormalities that should be addressed quickly include severe changes in mentation such as stupor, coma, hyperexcitability, delirium and seizures (see Chapter 9).

Immediate evaluation of the renal system should include assessment of the ability to urinate and palpation of the urinary bladder. This is particularly the case for cats, where urethral obstruction should be ruled out in all cats with vague clinical signs.

Animals with dysfunction in any one of the four major organ systems should be taken immediately to the treatment area for further evaluation and treatment.

Conditions affecting other body systems are generally not immediately life-threatening in themselves, but their effects on the four major organ systems can result in death. For example, a fracture of the femur is not life-threatening by itself, but the resultant blood loss into the thigh musculature may result in hypovolaemia and cardiovascular compromise. Problems that do not immediately affect the four major organ systems but require that the animal be taken immediately to the treatment area include:

- Recent ingestion of, or topical exposure to, a toxin
- Severe pain
- Recent seizures
- Trauma
- Excessive bleeding
- Prolapsed organs
- Snake bite
- Hyperthermia
- Open wounds
- Fractures
- Burns
- Dystocia
- Death.

If an owner is overly concerned, even if the animal appears physiologically stable, it should be taken to the treatment area for observation. Emergency assessment of patients conveyed directly to the treatment area then includes the primary survey and the secondary survey. Good communication with the owner throughout this time is paramount.

Primary survey

The primary survey amplifies the information obtained during triage. The purpose of the primary survey is to decide whether the patient is stable, and to identify and treat any immediate life-threatening conditions. The primary survey includes evaluation and support of the airway, respiratory system, cardiovascular system (poor tissue perfusion, control of haemorrhage) and central nervous system (level of consciousness). Evaluation of these parameters allows the clinician to identify any emergent life-threatening problems and classify the patient as stable or unstable. Any patient that cannot clearly be classified into either category should be considered unstable.

The primary survey comprises a more detailed evaluation of the same physical parameters as triage. Evaluation of the respiratory system includes: determination of whether the upper airway is patent (by observing the respiratory pattern whilst simultaneously auscultating the lungs to ensure normal air movement); evaluation of mucous membrane colour; and assessment of respiratory rate, rhythm and effort. The trachea and all areas of the thorax should be carefully auscultated. More objective information regarding respiratory function can be obtained from pulse oximetry, arterial blood gas analysis and end-tidal carbon dioxide measurement, although it is worth remembering that abnormal perfusion can adversely affect the accuracy of pulse oximetry and end-tidal capnography. Hypoxaemia can result in pansystemic problems due to poor oxygen delivery to the tissues, and requires immediate correction. Oxygen supplementation should be provided to any emergency patient if respiratory compromise is evident or suspected, and definitive treatment for the

cause of the respiratory compromise should be provided as soon as possible (see Chapter 7). Flow-by oxygen is the most effective means of increasing the inspired oxygen content while assessing a patient, although cats may benefit from time in a stress-free, oxygen-enriched environment such as an oxygen cage (Figure 1.2).

Assessment of tissue perfusion includes: evaluation of mucous membrane colour; capillary refill time; auscultation of the heart; and palpation of pulse rate, rhythm and quality. Core body temperature to toe web temperature may also provide additional information. More in-depth and objective evaluation of tissue perfusion and cardiovascular function could include arterial blood pressure measurement, electrocardiography and blood lactate concentration. More advanced cardiovascular monitoring modalities, such as central venous pressure determination, pulmonary artery catheter placement, and measurement of oxygen delivery and oxygen consumption, can be very useful during longer-term management of the critically ill patient, but are rarely, if ever, available at the time of triage. Clinical recognition of poor tissue perfusion such as pale or grey mucous membranes, prolonged or rapid capillary refill time, cold extremities and/or abnormalities of cardiac rate or rhythm warrants rapid identification of the underlying cause and definitive treatment (see Chapter 3). Prolonged hypoperfusion can cause changes in cellular metabolism that result in intracellular sodium and calcium accumulation, cell swelling, cell membrane damage, lipid peroxidation, release of detrimental oxygen-free radicals and cell death.

Extreme changes in the patient's mentation, such as stupor, coma or seizures, require rapid assessment for the underlying cause and immediate treatment to prevent irreversible changes, which can occur if prolonged seizures or hypoglycaemia causing central nervous system dysfunction is not treated rapidly. Similarly, increased intracranial pressure causing stupor or coma may progress if it is not managed promptly, resulting in herniation of the brain through the foramen magnum.

In summary, the primary survey assures identification and immediate treatment of life-threatening problems. It also allows identification of unstable patients so that appropriate monitoring can be instituted and potential problems can be anticipated and prevented.



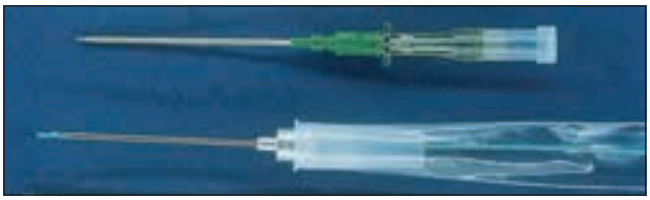
1.2 Critically ill animals have little physiological reserve to tolerate physical examination or medical intervention. Allow dyspnoeic animals to stabilize in oxygen before performing diagnostics and, above all, do no harm.

Secondary survey

After the primary survey and stabilization of immediate life-threatening conditions, the secondary survey is performed. This includes a full physical examination, including measurement of bodyweight if possible, obtaining a detailed history from the owner, assessment of the response to initial therapy, and more in-depth diagnostics, including clinical pathology and imaging procedures. It is during this time that a comprehensive diagnostic and therapeutic plan can be made and a cost estimate as well as prognosis can be formulated. In addition, the owner should be asked to choose the level of cardiopulmonary resuscitation to be performed should the animal suffer a cardiac or respiratory arrest (code status).

Vascular access

Intravenous access should be obtained in all critically ill patients for administration of intravenous fluids and drugs (Figure 1.3). Peripheral veins, such as the cephalic or lateral saphenous vein, are the most common vessels used for intravenous catheterization, mainly due to their accessibility and familiarity to most emergency personnel. Central venous access using the jugular or medial femoral vein allows higher drug concentrations to be achieved in the coronary vessels (important in cardiopulmonary resuscitation) and allows placement of a larger-diameter catheter. This generally facilitates more rapid fluid administration as long as the length of the catheter is not so long as to cause resistance to fluid flow. However, central vessels are more difficult to access compared with the peripheral vessels, making them a second choice in an emergency situation when vascular access must be rapid. If a catheter cannot be placed percutaneously, a cutdown procedure may be needed to obtain vascular access. Jugular venepuncture and catheter placement is contraindicated in patients suspected of having a coagulopathy or raised intracranial pressure. In neonates, the easiest and most expeditious way to obtain vascular access is via intraosseous catheter placement. Absorption of drugs via this route is almost as fast as central venous administration. Vascular access options are discussed in more detail in Chapter 2.



1.3 Intravenous access must be established as quickly as possible in the critical emergency patient. Short over-the-needle catheters (top) placed in peripheral veins are best, as the flow rate is optimal in a short wide-bore catheter. Long through-the-needle catheters (bottom) placed in central veins are ideal for longer periods of hospitalization.

Emergency database

Blood should be obtained for an emergency database in all critically ill patients as soon as possible after presentation. The minimum database should include measurement of packed cell volume (PCV) and refractometric total solids (TS) or total protein (TP), glucose, blood urea nitrogen (BUN) and evaluation of a blood smear. Assessment of

urine specific gravity prior to fluid therapy, and of serum sodium and potassium levels and acid–base status can provide valuable information for use in diagnosis and can facilitate appropriate therapy. Blood samples can be collected from the hub of the intravenous catheter as it fills with blood, or obtained from the hub of a 25 G needle placed into a peripheral blood vessel (Figure 1.4). The PCV, TP/TS, dipstick glucose, dipstick BUN and blood smear can all be obtained from three heparinized microhaematocrit tubes.



1.4 Blood samples for the emergency database can be obtained by filling a microhaematocrit tube from the hub of a 25 G needle placed in a peripheral blood vessel, in this case the cephalic vein.

Packed cell volume and total solids

PCV is used as a good estimate of haemoglobin (Hb) concentration (PCV divided by 3 approximately equals Hb (in g/dl – multiply this by 10 to get g/l)) and hence oxygen-carrying capacity. The only exception to this is if haemoglobin-based oxygen carriers (HBOCs) have been used. Although not available at the time of writing, they may become so in future. If HBOCs are used, the PCV will give a falsely low estimate of haemoglobin. In addition, HBOCs also lead to changes in serum colour and care must be taken when interpreting any colorimetric tests in these patients. Refractometer measurement of TS allows estimation of serum proteins, which provides a rough indication of plasma colloid osmotic pressure, thereby facilitating decisions about the type of intravenous fluids to be used. TS is not as accurate as an estimate of colloid osmotic pressure after the administration of synthetic colloids, as the value tends towards that of the synthetic colloid administered.

PCV and TS should be interpreted together, and in conjunction with clinical findings. They can provide information regarding hydration status, as well as an estimate of red cell content in the blood. Changes in these two parameters often parallel each other, but an alteration in the normal ratio of PCV to TS gives additional useful information. An increase in both PCV and TS is consistent with dehydration, as total body fluid loss results in concentration of red blood cells and plasma proteins. A decrease in PCV and TS is seen with aggressive fluid therapy or after haemorrhage. However, the decrease in both PCV and TS is not seen immediately following haemorrhage, as it takes time for fluid to shift from the interstitium to the intravascular space to cause dilution. In addition, immediately following an acute loss of blood volume in the dog, splenic contraction causes an influx of erythrocytes into the circulation in an attempt to restore circulating volume and increase oxygen-carrying capacity of the blood, improving tissue oxygen delivery. Thus, following acute blood loss, the initial PCV may be normal or even increased, accompanied by a decreased TS due to interstitial fluid shifts diluting the plasma proteins. When faced with a trauma patient that has a normal PCV but decreased TS, there is a strong possibility that significant haemorrhage has occurred.

A decrease in PCV with a normal TS suggests an increase in destruction or a decrease in production of red blood cells. A decreased PCV with haemolysed or icteric serum suggests haemolytic anaemia, although hepatic and post-hepatic causes of icterus cannot be ruled out. Anaemia of chronic disease and bone marrow disorders that cause non-regenerative anaemia are characterized by a decreased PCV with a normal TS.

An alteration in the PCV:TS ratio characterized by an increased PCV but a normal to decreased TS can be seen with severe dehydration accompanied by concurrent protein loss. The most profound example of this occurs in patients with severe haemorrhagic gastroenteritis, which can have a PCV of 70% or higher, but a normal TS. Hypoproteinaemia (low TS) can result from haemorrhage, inflammation (e.g. peritonitis) or loss of protein from the body through the gastrointestinal tract or kidney. Loss through the kidney (protein-losing nephropathy) results in hypoalbuminaemia, whereas a loss from the gastrointestinal tract (protein-losing enteropathy) results in panhypoproteinaemia. An increase in PCV with a normal TS is seen in patients with polycythaemia, which is relatively rare. Figure 1.5 lists the possible causes of alterations in PCV and TS.

PCV (%)	TS (g/l)	Possible causes
Increased	Increased	Dehydration
Increased	Normal	Normal for breed (e.g. Greyhound); polycythaemia; dehydration combined with protein loss
Normal	Increased	Hyperglobulinaemia; anaemia with dehydration
Normal	Decreased	Acute haemorrhage, hypoalbuminaemia
Decreased	Normal	Haemolytic anaemia, non-regenerative anaemia
Decreased	Decreased	Haemorrhage, concurrent anaemia and hypoproteinaemia

1.5 Changes in packed cell volume (PCV) and total solids (TS) expected with different disease states.

PCV and TS are important in guiding fluid and diuretic therapy. The absolute values determine the choice of fluid (e.g. isotonic crystalloid, colloid, blood products) to be delivered when correcting hypovolaemia or dehydration (see Chapter 4). A change in PCV and TS is expected following aggressive fluid or diuretic therapy, and these parameters should be measured frequently to help monitor response.

Physical appearance of blood samples

Examination of the microhaematocrit tube following centrifugation can provide additional information. A large buffy coat indicates a high white blood cell count. The colour of the serum may provide clues to the disease process; icterus may be due to pre-hepatic, hepatic or post-hepatic problems. Lipaemic serum may be due to pancreatitis, post-prandial lipaemia, or may be associated with hyperadrenocorticism or hypothyroidism. Haemolysed serum may be due to the collection technique or intravascular haemolysis.

Blood glucose

Increased blood glucose may be due to insulin resistance and/or lack of insulin (diabetes mellitus), or acute glycogenolysis. Insulin resistance and glycogenolysis due to stress are seen most commonly in cats, but can also occur in dogs secondary to head trauma, seizures, severe hypovolaemia or hypoxia. The hyperglycaemia in these cases is transient if the underlying problem is corrected (e.g. fluid resuscitation if hypovolaemic). In contrast, although blood glucose levels will decrease slightly following intravenous fluids in a patient with diabetes mellitus, hyperglycaemia will persist in a diabetic patient unless it receives insulin therapy. Serum or urine ketones should be measured in patients presenting with high blood glucose, especially if they have a metabolic acidosis. Ketones can be demonstrated in the plasma from the microhaematocrit tube using ketone dipsticks, which can detect acetone and acetoacetate but not β-hydroxybutyrate.

Hypoglycaemia is a common finding in the emergency patient. It can be identified in patients with insulin overdose, sepsis, hypoadrenocorticism, juvenile hypoglycaemia, heatstroke, severe hepatic dysfunction, insulin-secreting tumours, insulin-like growth factor-secreting tumours, severe hypothermia and storage diseases. When using a glucometer or dipstick, falsely low results are obtained for glucose in whole blood when the PCV is high. This variation differs with each manufacturer. A more accurate result can be obtained by centrifuging the blood sample and measuring the serum glucose levels.

Blood urea nitrogen

BUN can be estimated using a dipstick. Although this method has limitations, when performed correctly it is a very useful screening test. A low dipstick BUN is accurate, but elevated results should be confirmed by other laboratory methods. Increased BUN may result from pre-renal, renal or post-renal causes, while low BUN can occur due to severe liver dysfunction or diuresis.

Blood smear

The red blood cells, white blood cells and platelets should be evaluated using a carefully prepared blood smear. The number and morphology of each cell type should be evaluated and recorded. Examination of the red blood cells is most important in patients with anaemia or if there is a suspicion of blood loss. Signs of regeneration such as polychromasia or anisocytosis help to characterize the anaemia as regenerative or non-regenerative. Cell morphology should be evaluated for the presence of spherocytes (seen in patients with immune-mediated haemolytic anaemia), Heinz bodies (indicating oxidative damage to haemoglobin), schistocytes (suggesting intravascular shear injury) or echinocytes (can be seen after rattlesnake envenomation). Parasites such as *Mycoplasma haemofelis* or *Babesia* spp. may also be seen (see Chapter 13).

The blood smear should be scanned at low power to estimate the number of white blood cells, and then at higher power to assess their morphology. One white blood cell viewed per X40 field at the feathered edge approximates to a cell count of 1.5 x 10^9/l. The differential count and nucleated cell morphology can be assessed using oil immersion. Leucocytosis with a mature neutrophilia suggests a stress response, or an inflammatory or infectious process. Immature neutrophils such as band cells and occasionally metamyelocytes or myelocytes may be released into the circulation, termed a 'left shift', if there is a severe inflammatory or infectious process. However, the absence of a leucocytosis or a left shift does not rule out inflammation or infection. Leucopenia can be due to decreased production or sequestration of white blood cells. Decreased production can result from viral infections such as parvovirus, or from the administration of chemotherapeutic or immunosuppressive drugs. White blood cell sequestration resulting in leucopenia occurs in patients with severe infections or extensive tissue necrosis, for example those with peritonitis, necrotizing pancreatitis or bite wounds. Transient leucopenia can also be seen in hypothermic patients.

Bleeding patients should be evaluated for adequacy of platelet numbers. The whole slide should be scanned under low power for platelet clumps, since these can result in an artificially low count. In healthy dogs and cats there should be 11–25 platelets per monolayer field under oil immersion. One platelet viewed per oil immersion field (X100) approximates to 15 x 10^9/l (i.e. three platelets per oil immersion field approximates to 45 x 10^9/l in the blood). Most patients with spontaneous bleeding due to thrombocytopenia have fewer than two platelets per oil immersion field; animals with four to five platelets per field are unlikely to be bleeding due to thrombocytopenia. Low platelet numbers can result from decreased production, consumption or increased destruction.

Summary

The amount of information obtained from a simple emergency database can be tremendous, and should not be underestimated. This information, combined with a thorough history and physical examination, can often provide a diagnosis as well as a prognosis.

Acid–base status and electrolytes

Cage-side blood gas, acid–base and electrolyte monitors are becoming more widely available for veterinary surgeons. Monitors differ, but can provide objective data pertaining to acid–base status, oxygenation, ventilation and electrolytes. Some monitors can also analyse lactate, renal parameters and glucose, whilst newer machines may be equipped with co-oximetry. Analysis typically requires between 0.2 and 0.5 ml of whole blood, which is either inserted directly into the analyser (which contains all the reagents) or is injected into a cartridge that is inserted into the analyser. Different cartridges allow the clinician to choose the parameters to be measured, or the monitor can be programmed to perform selected analyses. Identification of acid–base and electrolyte derangements (see Chapter 5) can expand on the history, physical examination and emergency database, to further develop the problem list and emergency plan.

Cage-side ultrasonography

Ultrasonography is becoming more widely available as a cage-side tool for emergency patients. The techniques originate from the use of FAST (focused assessment with sonography for trauma) scans in human emergency medicine and the range of point-of-care ultrasound (POCUS)

techniques used in veterinary medicine is expanding. The goal is not to perform a comprehensive full body cavity scan, but to answer specific questions. The most common use is to detect fluid within a cavity, such as free abdominal fluid. A free fluid scan should be performed on all trauma patients within minutes of presentation, and any animal with an acute abdomen. Furthermore, because free abdominal fluid can develop following fluid resuscitation, it should be repeated as necessary. Figure 1.6 illustrates how to use ultrasonography to detect free abdominal fluid in an emergency setting. Fluid may also be detected within the pericardial and pleural spaces if effusion is suspected based upon physical examination. Cage-side ultrasonography can also be used to identify the presence/absence of a bladder, for the detection of pyometra and in the assessment of fetal health.

- Cage-side ultrasonography should be performed with the patient in lateral recumbency
- Four different sites should be evaluated in two planes (longitudinal and transverse):
  - Gravity-dependent flank to detect fluid around the spleen, intestines and kidneys
  - Gravity-independent flank to detect fluid around the spleen, intestines and kidneys
  - Ventral midline subxiphoid to detect fluid between the liver lobes
  - Ventral midline prepubic to detect fluid around the urinary bladder
- If fluid is detected, abdominocentesis should be performed and the fluid analysed

1.6 Use of cage-side ultrasonography to detect abdominal fluid in an emergency setting.

Emergency plan

The emergency plan depends upon the presenting problem and stability of the patient, and the level of nursing and technical support available. A medical problem list should be generated and the problems prioritized from the most to the least life-threatening. The problems should then be addressed in that order, making a diagnostic, therapeutic and monitoring plan for each one. The plans for each problem should be collated and a comprehensive, concise and clearly written hospital order list should be formulated. Categories that should be covered include fluid therapy, medications to be administered, diagnostics to be performed, parameters to be monitored, code status and nursing orders.

Fluid therapy

Fluid therapy orders should include the type of fluid to be administered, the rate of infusion and the route by which the fluid should be given. The frequency of reassessment of the fluid orders depends upon patient stability and how rapidly the fluid requirements change. In very unstable patients, fluid therapy may require re-evaluation every 15–30 minutes, depending on the response to therapy. Relatively stable patients, where fluid deficits are being replaced over 24 hours, require less frequent reassessment of fluid orders, perhaps as infrequently as every 6–12 hours. Fluid rate and type are determined not only by cardiovascular status but also by sodium and potassium concentrations. Type of fluid and rate of infusion become very important in patients with extremes of sodium concentrations, such as severe hyponatraemia or hypernatraemia. In these cases, fluid therapy orders may need to be changed hourly depending upon the desired rate of sodium concentration change and the response to therapy (see Chapter 5). Dextrose, potassium or other electrolytes may need to be added to the fluid bags, but these supplemented fluids should never be administered as a bolus. Synthetic colloids or even blood products may need to be administered if severe hypoproteinaemia or anaemia has been identified on the emergency database.

Medication

The types of medication and the dose, route, rate and frequency of administration should be clearly written and reviewed with the individual who will be administering the drugs. All drugs that are being administered should be reviewed for incompatibility with each other, as well as potential adverse effects in specific patients or disease processes. If side effects of a certain drug are of particular concern, specific information about the side effects should be noted in the treatment orders, and the parameters to monitor and suggested therapy for adverse reactions should also be included in the record.

Diagnostic plan

The diagnostic plan should be written and tests listed in priority of importance for the emergency care of the patient. The stability of the patient as well as the importance of the information that the test will provide should be considered when requesting a diagnostic test. The question that should be asked for each test should be: 'Will the information that I obtain make a difference to what I do on an emergency basis?' If the answer to this question is 'no', then the test should not be performed. Certain blood tests and urine specific gravity in which pre-treatment values may be helpful later are the exception to this rule.

Monitoring

Monitoring procedures should be listed and clinician notification criteria should be clearly communicated and reviewed with the nursing personnel. Often, the trend of change in a parameter is more important than the absolute value. Monitoring trends of change allows anticipation of problems before they occur. Monitoring parameters may be divided into physical examination, clinicopathological data and electronic evaluation.

Physical examination parameters should include:

- Mucous membrane colour
- Capillary refill time
- Pulse rate and quality
- Heart rate
- Lung sounds
- Respiratory rate and effort
- Neurological function
- Urination and urine output
- Defecation
- Vomiting
- Rectal temperature
- Abdominal pain
- Observation of skin and mucous membranes for ecchymoses and petechiations
- Assessment for peripheral oedema or interstitial dehydration
- Assessment of volumes of fluid collected from chest tubes or drains.

The most common clinicopathological parameters monitored in the emergency room include:

- PCV
- TP/TS
- Glucose
- Dipstick BUN
- Serum sodium concentration
- Serum potassium concentration
- Blood gas analysis
- Lactate
- Urinalysis
- Blood smear
- Clotting times (prothrombin time (PT) and activated partial thromboplastin time (aPTT)).

Electronic monitoring may include:

- Continuous electrocardiography
- Blood pressure measurement (Doppler, oscillometric or direct methods)
- Pulse oximetry
- End-tidal capnography
- Detection of free abdominal fluid using ultrasonography
- Measurement of central venous pressure
- Cardiac output
- Oxygen delivery
- Oxygen consumption.

Nursing orders

Nursing orders should be tailored to the needs of each individual patient. The specific disease process, the severity of the patient's condition and the level of staffing should all be considered when orders are written. For example, one nurse cannot provide comprehensive nursing care to a comatose, 50 kg large-breed dog that is being mechanically ventilated and receiving peritoneal dialysis.

The emergency plan must take into account the needs of the patient, the client's needs and financial capabilities, the immediate and overall prognosis and the capabilities of the emergency staff and facility (Figure 1.7). If it is recognized that the best emergency plan cannot be accommodated by the facility and staff, referral of the patient to a tertiary facility that can provide optimal care should be considered.

Cardiovascular

- Electrocardiography
- Blood pressure monitoring (direct and indirect)
- Central venous pressure monitoring
- *Defibrillator with internal and external paddles*
- Fluid pumps and syringe drivers
- Pressure bags for rapid fluid administration
- Selection of intravenous catheters

Respiratory

- Means to provide short- and long-term oxygen therapy (e.g. oxygen cage, face masks)
- Means to intubate and ventilate (e.g. laryngoscope, endotracheal tubes, Ambu resuscitation bag)
- Pulse oximeter
- End-tidal capnograph

Diagnostics

- Glucometer (dextrometer)
- Means to measure TP/TS and PCV
- Microhaematocrit tubes, centrifuge, refractometer
- Microscope, slides, stain (Diff-Quik® and Gram) and immersion oil
- Electrolyte and blood gas analyser
- Lactate analyser
- Coagulation analyser
- Snap tests (e.g. feline leukaemia virus, feline immunodeficiency virus, parvovirus)
- *Osmometer*
- *Colloid oncotic pressure analyser*
- Urine dipsticks
- Dipsticks for BUN and ketones
- X-ray machine, processor and view box (or digital radiography)
- Ultrasound machine

Surgical

- Anaesthetic machine
- Surgical gowns and drapes
- Surgical sets
- Electrocautery
- Surgical table and lights
- Chest tubes, tracheostomy tubes

Other

- Weighing scales
- Thermometer
- Means of providing warmth
- Ophthalmoscope
- Otoscope
- Pen light
- Stomach tubes

1.7 Recommended emergency room equipment. Those in *italics* are desirable but not essential.

Chapter 2

Vascular access

Sophie Adamantos

The placement and maintenance of intravascular access is one of the most important skills for any veterinary surgeon (veterinarian) and veterinary nurse working in emergency and critical care medicine. Rapid and accurate placement of appropriate intravenous catheters allows administration of fluid and drug therapy, as well as providing an atraumatic means for serial blood sampling. Furthermore, placement of specialized catheters (e.g. central venous or arterial) can assist in monitoring intravascular volume status and blood pressure. Familiarization with alternative routes of vascular access can be important in particular situations, for example intraosseous access in collapsed kittens and puppies. This chapter addresses the different types of vascular access (catheter placement and maintenance) and summarizes complications that may occur.

Intravenous access

A number of factors should be considered when choosing the optimal type of intravenous access for each individual animal. These include:

- Vein selection and preparation
- Catheter choice, including material, length and gauge
- Ease of insertion
- Ease of maintenance, monitoring and prevention of complications.

Vein selection

When choosing the site for catheter placement a number of questions should be considered:

- Why am I placing this catheter?
- How long will it remain in place?
- What will I be administering through it?
- Does the animal have any medical or behavioural factors that should be considered?

The last question may include consideration of the animal's temperament (aggressive animals may prove difficult to manage with a jugular catheter), the presence of coagulopathy (a contraindication for use of the jugular vein) and potential sources of catheter contamination (e.g. local tissue damage, skin infection, presence of vomiting, urination, diarrhoea and excessive salivation). Animals with regional vascular obstruction (e.g. gastric dilatation–volvulus or saddle thrombus) should have catheters placed in the front legs (i.e. at a site that is not affected by the obstructed vessel).

In emergency patients, the initial catheterization site should be chosen to facilitate rapid and effective catheter placement. Peripheral veins are generally more suitable than the jugular vein. Catheterization via a peripheral vein is adequate for administration of most fluids and medications, and should be the primary site for rapid intravenous access in the majority of emergency patients. There are several suitable peripheral sites in the dog and cat, including:

- Cephalic vein and accessory cephalic vein (below the carpus)
- Medial and lateral saphenous vein
- Auricular veins in breeds with large ears (e.g. Basset Hound)
- Dorsal common digital vein (over the metatarsal bones).

Most commonly the cephalic vein is used as it is familiar and most animals will tolerate gentle restraint for catheter placement while in sternal recumbency. It is important to be familiar with other readily accessible sites, especially when faced with small patients or those that have suffered trauma to multiple limbs.

Following initial vascular access and fluid resuscitation via a peripheral vein, a decision should be made as to whether the animal is an appropriate candidate for central venous catheterization. Central veins are large veins that lie within the thoracic or abdominal cavity. They can be accessed from more peripheral sites including the jugular and saphenous veins. Factors that may prompt placement of a central venous catheter include:

- Likely long-term (>5 days) administration of fluids
- Administration of hypertonic fluids or medications
- The need to obtain multiple venous blood samples
- Necessity or preference for measuring central venous pressure (CVP)
- Animal factors (e.g. conformation, temperament) suggesting that maintenance of a peripheral catheter may be challenging.

The jugular vein is the most frequently used site for placement of central venous catheters and is easily accessible in most animals. Other sites may be used to access the central compartment, most commonly the medial saphenous vein, which is particularly useful in cats. Hyperosmolar fluids (such as >5% glucose infusions or parenteral nutrition) should always be administered via a

BSAVA Manual of Canine and Feline Emergency and Critical Care, third edition. Edited by Lesley G. King† and Amanda Boag. ©BSAVA 2018

central catheter to reduce the risk of thrombophlebitis. Any catheters (or ports of multi-lumen catheters) used for parenteral nutrition should be reserved for that purpose only and strict asepsis should be observed when managing the catheter. If these catheters are to be used to measure CVP, a jugular catheter is preferred. The tip of the catheter should lie within the thoracic cavity and the catheter tip on a lateral radiograph needs to be between the caudal aspect of the second rib and the right atrium. Placement should be checked with thoracic radiographs. Although CVP can be measured from the caudal vena cava, the cranial vena cava is preferred in dogs and cats.

Catheter selection

A large number of catheters are available on the veterinary and human medical markets, making selection difficult and at times confusing. Catheter size, composition and placement method are the predominant characteristics to be considered in catheter selection.

Fluid flow rate through a catheter is related to both the length and radius of the catheter as well as rheological factors. Of these, catheter radius (r) has the greatest effect, flow rate being related to r^4. A reduction in catheter diameter by half results in a 16-fold decrease in flow rate, whereas doubling of the diameter would result in a 16-fold increase in maximum flow. Increasing catheter length also results in decreased flow due to increased resistance. When choosing a catheter for rapid fluid resuscitation the shortest catheter with the biggest radius (gauge) should be utilized.

Catheters are made from a variety of chemically inert materials in order to limit vessel irritation; once they are in the body, however, inflammatory reactions may occur due to agents used in the manufacturing process. Silicone and polyurethane are minimally reactive, making these materials ideal for use in long-term catheters. Silicone is thought to be particularly desirable due to its additional characteristic of flexibility but is very expensive. In contrast, Teflon® (polytetrafluoroethylene) has intermediate reactivity and is relatively stiff, making it less suitable. Antibiotic-impregnated catheters have been introduced to the human and veterinary markets; however, there are currently insufficient data to recommend their use in veterinary patients given the significant additional cost. Many catheters are rendered radiopaque by the addition of barium or bismuth salts into the plastic.

Catheters can be broadly divided into a number of categories by their placement method:

- Butterfly or winged-needle catheters
- Over-the-needle catheters
- Through-the-needle catheters
- Peel-away catheters
- Over-the-wire catheters (Seldinger technique).

Butterfly catheters (Figure 2.1) are essentially needles with attached wings, which enable them to be secured, and a short extension tube that facilitates attachment of a syringe for collection of blood or administration of intravenous medications. They are manufactured in a variety of gauges and lengths. Butterfly catheters are not suitable for fluid therapy as the sharp tip will damage the vein if it is left in place for more than a few minutes.

Over-the-needle catheters (Figure 2.2) are the most common catheter type in day-to-day use in veterinary practice. They are suitable for short- to medium-term intravenous access. Insertion is technically easy and associated with few complications. The catheters are inexpensive and



2.1 Butterfly needles are suitable for short-term vascular access to deliver anaesthetic agents or intravenous medications.



2.2 Over-the-needle catheters are easily placed in peripheral veins and suitable for short- or longer-term administration of drugs or fluid therapy.

there are few contraindications to placement. They comprise a rigid, typically metal, stylet with a closely associated catheter fitted over it. The catheter should not be taken off the stylet prior to placement in order to prevent damage to the catheter. The stylet is used to penetrate the vessel and guide the tip of the catheter into the vein. The catheter is then slid off the stylet into the lumen of the vein. The catheters are generally made of stiff material (e.g. fluorinated ethylene propylene, FEP® or other fluorinated polymers) to prevent damage to the tip as it passes through the vessel wall. A wide variety of gauges and lengths is available, making them extremely versatile. There are a large number of companies that provide intravenous catheters to the veterinary and medical fields (see Useful websites below).

Through-the-needle catheters (Figure 2.3) have a large-bore needle which is placed into the vein, with an adjustable length catheter that is threaded through the needle into the vessel lumen. After successful introduction of the catheter, the needle is withdrawn from the vessel and either enclosed in a plastic guard or removed altogether. If the needle is removed an adaptor is attached to the end of the catheter that remains outside the vein, and the catheter is secured. These catheters are easy to place and are a relatively affordable way of accessing the central venous compartment. However, the presence of the introducer



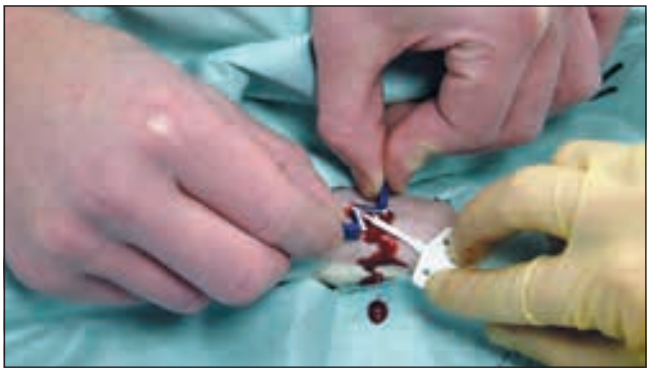
2.3 An example of a through-the-needle catheter with attached introducer and needle guard.

needle and guard make some of these catheters difficult to secure and can result in bulky dressings.

Peel-away catheters (Figure 2.4) have a plastic guide (or sheath) which is placed in the lumen of the vessel using an over-the-needle technique. The needle is then removed and the catheter is inserted through the guide. The guide can then be 'peeled away' by pulling gently outwards and upwards on the two tabs of the sheath. The gauge of the catheter is limited to that of the plastic guide.

The final group of catheters are those designed to be placed by the over-the-wire (Seldinger) technique (Figure 2.5); they are placed using a wire guide. A needle or introducer catheter is inserted into the vein and a wire is passed through it. The introducer catheter is removed, leaving only the wire in place. The catheter is then advanced over the wire into the vessel lumen. Theoretically, any gauge of catheter may be placed. In some circumstances this is aided by use of a vessel dilator advanced over the wire prior to catheter placement, which increases the diameter of the subcutaneous tunnel and venous puncture site. These catheters are secured by suturing them to the skin at the entry site via wings. Placement is shown in Figure 2.6.

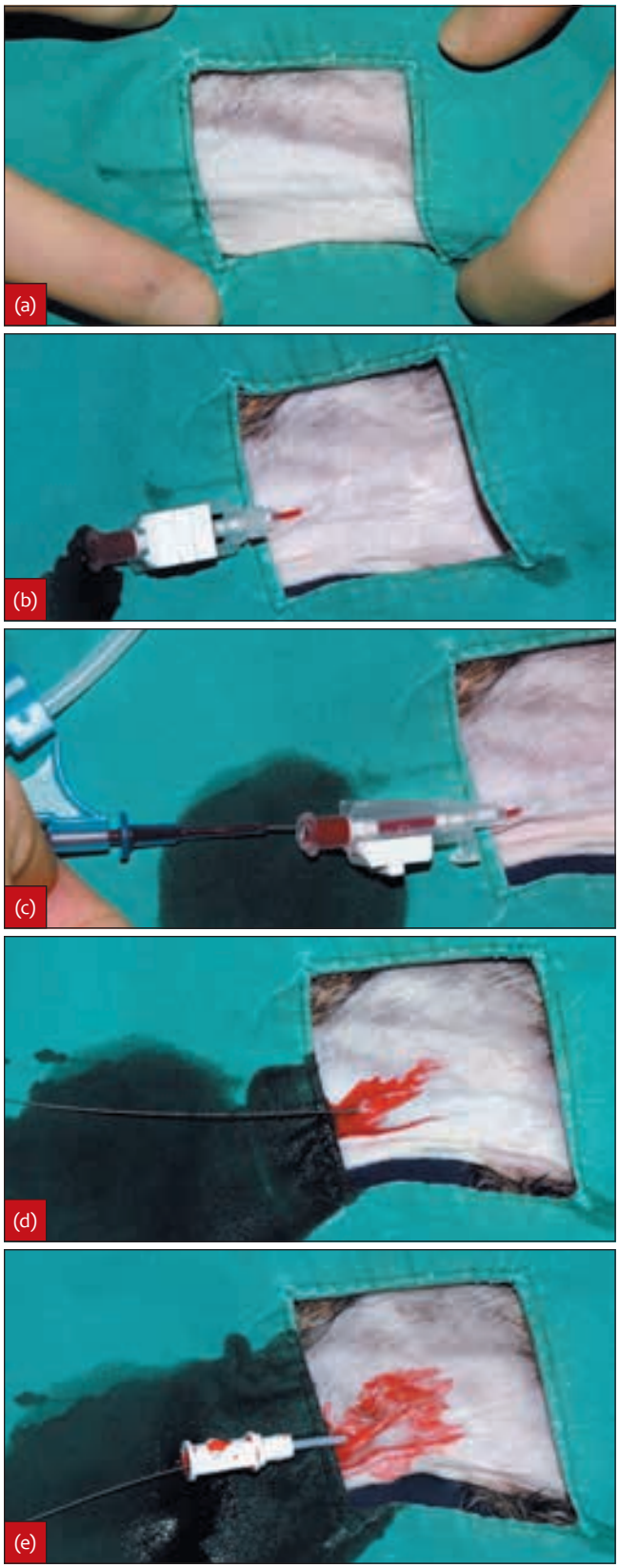
Peel-away and Seldinger technique catheters are available as single or multi-lumen catheters. Multi-lumen catheters have several ports (typically two or three), each running via a separate channel to the tip of the catheter, thus preventing mixing of fluids/drugs until they reach the bloodstream. The use of a multi-lumen catheter should be considered if the animal requires a mixture of fluid therapy, drug therapy, parenteral nutrition, CVP monitoring and/or repeated blood sampling (see Chapter 25).



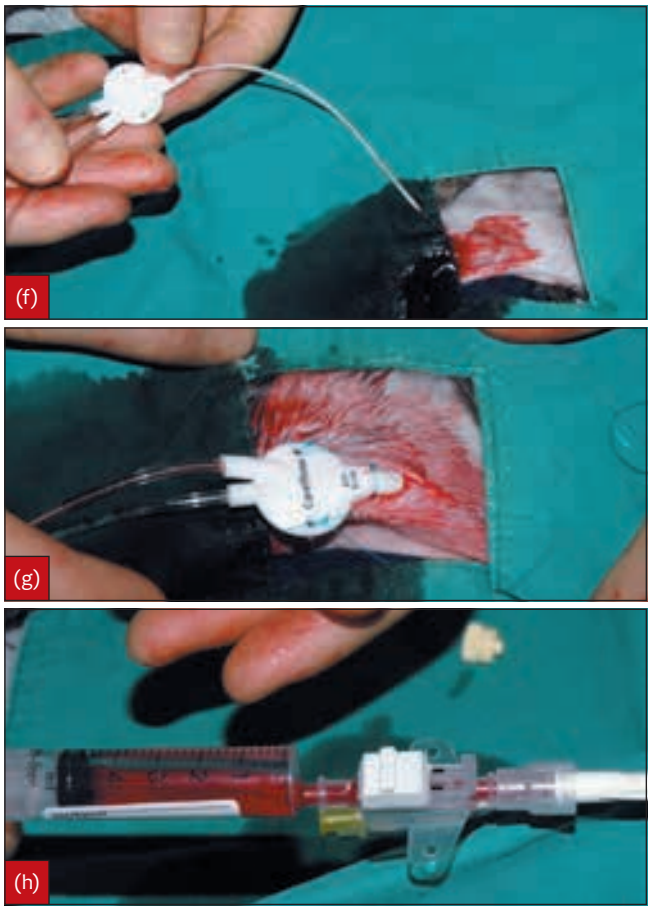
2.4 An example of a peel-away catheter. (Courtesy of E Leece)



2.5 An example of a catheter kit which utilizes an over-the-wire (Seldinger) placement technique.



2.6 Placement of a central line in the jugular vein using the Seldinger (over-the-wire) technique. (a) The area is surgically prepared and draped. (b) A facilitative skin incision is made and a large introducer needle or catheter placed into the vein. In this case an introducer catheter with flow switch is used. (c) A long wire is inserted through the introducer needle/catheter. (d) The needle/catheter is removed, leaving the wire in place. (e) A dilator is passed into the vein over the wire to enlarge the subcutaneous tunnel. The dilator is then removed. Note that some central vein catheters do not require use of a dilator as the catheter itself has a 'self-dilating' tip. The manufacturer's instructions should be followed. (continues)



2.6 (continued) Placement of a central line in the jugular vein using the Seldinger (over-the-wire) technique. (f) The catheter is advanced into the vein over the wire. The wire is then removed. (g) The catheter is sutured into place. (h) Blood is withdrawn from each port of the catheter into a syringe prefilled with heparinized saline to guarantee intravascular placement. The ports are then flushed and the catheter bandaged carefully in place.

1. Hand washing and hygiene should be performed before placement. Sterile gloves are not necessary for short-term peripheral catheter insertion. The skin overlying the vein should be prepared with an antimicrobial scrub solution and surgical spirit.
2. The vein should be raised by an assistant.
3. The catheter can usually be placed directly through the skin but in some patients, a **small** facilitative skin nick made with a No. 11 blade may ease insertion. This is especially useful in dehydrated animals or those with very thick skin, and prevents burring of the catheter tip as it passes through the subcutaneous tissues.
4. The catheter is advanced through the skin into the vein at a 30–40 degree angle with the stylet bevel up.
5. Once blood is visualized in the flash chamber, the stylet and catheter are flattened (i.e. the angle between the catheter and limb is reduced). The catheter/stylet unit is then advanced a small distance further into the vein to ensure the catheter lies fully within the lumen.
6. The catheter is advanced off the stylet. The stylet should remain absolutely immobile as the catheter is advanced.
7. Once the catheter has been fully advanced, the stylet is removed and discarded. If problems are encountered whilst advancing the catheter, flushing gently with heparinized saline may help. The catheter should never be pulled back on to the stylet as this may damage the catheter tip or shear off part of the catheter.
8. Once the catheter has been advanced into the vein the assistant can occlude the vessel by applying pressure over the vein at the distal end of the catheter to prevent spillage of blood.
9. A T-port or injection cap should be attached to the catheter and the catheter secured in place with adhesive tape.

2.7 Placement of a peripheral catheter.



2.8 An example of an extension set.

Catheter insertion

Peripheral veins

A large area of skin surrounding the vein should be clipped before insertion of the catheter. Long hair (feathers) on the caudal aspect of the limb may need to be removed if it will interfere with securing the catheter and to help prevent contamination. In some dogs a complete 360-degree clip of the limb may be necessary. Catheters should be placed aseptically and as distal in the vein as possible to allow subsequent venepuncture at a more proximal site. In the emergency situation there may not be time for full aseptic preparation of the vein. In these circumstances, potentially contaminated catheters should be replaced as soon as possible. Peripheral catheter placement is described in Figure 2.7.

A T-port or extension set should be attached and the catheter well secured with conforming non-elastic adhesive tape or sutures. Extension sets are useful as they prevent unnecessary blood loss, provide a method of closure when the catheter is not in use and increase the ease of connection of drip lines and drug administration (Figure 2.8). Needle-free bungs should be used to close the extension set ports. These are useful to minimize contamination associated with connection and disconnection as they can always remain in place, and many modern ones prevent movement of blood into and out of the catheter hub (zero displacement), which reduces infection risk. It is recommended that they are vigorously cleaned for 30 seconds with a sterile alcohol wipe, and then allowed to dry prior to reconnection or use for injections. Needle-free bungs should not be removed prior to attaching a giving set as fluids will run freely through them. Needle-free bungs also offer health and safety benefits for veterinary personnel because of reduced risk of accidental needlestick injuries. After placement of the initial non-elastic adhesive tape, the catheter should be bandaged in place to prevent contamination. This bandage should comprise a soft primary layer and a protective secondary layer.

Central veins

The most commonly used site for central venous access is the jugular vein. As a catheter of any length may be placed using the through-the-needle technique, other sites (e.g.

the medial saphenous vein) may also be utilized. Central venous catheters should be placed using strict aseptic technique. Sterile gloves should be worn and the catheter site should receive full surgical preparation and be draped appropriately before catheter placement. Although central lines may be placed in conscious animals if they are weak or debilitated, sedation or anaesthesia is required in most animals to prevent movement during the procedure. Considering the site and size of needle utilized, it is prudent to check for the presence of coagulopathy or thrombocytopenia before placement. In breeds predisposed to von Willebrand's disease a buccal mucosal bleeding time should also be performed.

Central lines may be placed using either the Seldinger (see Figure 2.6), through-the-needle or peel-away technique, as described above. These catheters are sutured in place and bandaged securely to prevent contamination and inadvertent removal. Peripherally inserted central catheters (PICC) are useful when access to the jugular vein is limited. In these cases long catheters are inserted through peripheral veins (usually the saphenous vein) into the caudal vena cava. These catheters can be used in the same way as conventional central catheters, although it must be remembered that if they are to be used to measure CVP then the tip of the catheter must be in the abdominal portion of the caudal vena cava. Recently, ultrasound-guided placement of central lines has been described in dogs (Chamberlin *et al*., 2013). This is associated with a steep learning curve, but may be useful in challenging cases.

Catheter maintenance

Maintenance of the catheter is vitally important; the catheter should be examined at least twice daily. The site of insertion should be monitored for signs of heat, erythema, swelling, pain (on palpation or during injection) or leakage of fluid. The leg and foot should be checked for swelling above the catheter site (indicating extravasation of fluid) and swelling of the toes (indicating that the bandage or tape is too tight). Jugular catheters are usually sutured in place and therefore only need to be covered with a light bandage, avoiding application of too much pressure to the neck. Too tight a jugular wrap will rapidly result in swelling of the head or upper airway obstruction. It should be possible to pass a hand comfortably under the bandage after placement. The bandage should be removed and replaced each time the catheter is checked. If signs of phlebitis are present (redness or discharge at the catheter site, thickening along the length of the catheter when it is palpated under the skin) or the animal develops unexplained pyrexia, the catheter should be removed and the tip sent for microbiological culture. Routine use of topical or systemic antibiotic ointments is not recommended.

Catheter patency should be maintained by any fluid running through it. If the catheter is not being used continuously, intermittent flushing with saline or heparinized saline (1 IU of heparin per ml of saline) should be performed two or three times a day as well as before and after use. There is no benefit associated with the use of heparinized saline as opposed to normal saline for maintaining catheter patency in dogs or humans (Schallom *et al*., 2012; Ueda *et al*., 2013). In low use situations, it is more cost-effective and safer to use small bottles of normal saline because bags of heparinized saline contain no preservative and therefore have a short shelf-life. Palpation during injection can be used to ensure patency of peripherally placed catheters, but this is not possible in central veins. To check patency of central catheters, negative suction should be applied and a 'flash' of blood should be observed prior to flushing or using the catheter. Failure to obtain blood when a central line is aspirated can indicate that the catheter is no longer correctly placed in the vein or that there is a partial obstruction, e.g. thrombus at the tip of the catheter. Some smaller-gauge central catheters, however, function poorly for blood sampling from the outset. Correct placement can be confirmed by injecting a small amount of an intravenous radiographic contrast agent and obtaining radiographs. Replacement of central catheters should be considered if it is not possible to aspirate blood even if the fluids appear to be flowing well.

Once the catheter is no longer required it should be removed. As long as careful monitoring is performed, catheters may be left in place for several days; it is not recommended that catheters that are working well are replaced simply due to time elapsed since placement. When a catheter is not in use, needle-free valves or sterile injection caps (Figure 2.9) should be used to close access ports; ports should never be left open to the air. In order to reduce the risk of contamination of the catheter, disconnection of fluid lines should be avoided and only done when absolutely necessary. The use of needle-free valves is thought to minimize this risk. Central venous catheters are useful for blood sampling. A technique for sampling from catheters is described in Figure 2.10.



2.9 Examples of needle-free injection caps and closed caps.

Equipment

- 1 x 5 ml syringe containing 1 ml of heparinized saline (or flushed with unfractionated saline)
- 1 x 5 ml syringe for obtaining blood sample
- 1 x 5 ml syringe containing normal saline flush
- Syringe caps
- Blood tubes
- Alcohol swabs

Technique

- Swab the port through which the sample is to be taken. In multi-lumen catheters choose the largest bore channel port.
- Using the syringe containing heparin withdraw 3–5 ml of blood, cap the syringe and place aside (this ensures the sample is not contaminated or diluted).
- Obtain blood sample and place into tubes as required.
- Replace withdrawn blood.
- Flush catheter with saline.

2.10 Obtaining blood samples from a central venous catheter.

Catheter complications

Catheter displacement/extravasation of fluids or medications

Even with diligent efforts to secure and maintain catheters properly, there is a risk of displacement of any intravenous or arterial catheter. Risk of displacement may be greatest with the use of peripheral over-the-needle catheters. Careful securing and diligent monitoring are the best strategies to limit catheter migration and subsequent extravasation of fluids or medications.

Phlebitis/thrombophlebitis

All patients are at risk for phlebitis or thrombophlebitis by virtue of the inherent endothelial damage and inflammation incited by the presence of any intravenous catheter. Phlebitis may be simply inflammatory, or may be associated with concurrent infection because the catheter entry site and attached fluid administration set represent an important portal for bacterial entry. As discussed above, catheters should be checked regularly and if examination of the catheter insertion site or vessel identifies any redness, swelling, pain, firmness or other signs of inflammation such as pyrexia, immediate removal of the catheter should be considered. In addition, removal of the catheter should be considered if the animal shows evidence of pain on injection. The presence of phlebitis increases the risk of other more serious catheter-related complications such as endocarditis.

Thrombosis/thromboembolism

Continuous administration of intravenous fluids and/or regular intermittent flushing decreases the risk of thrombosis but does not completely prevent it. Blood clots may occur within the catheter lumen, obstructing flow, or between the catheter and the vessel wall. Thrombi that form outside the catheter or attached to the tip of the catheter may not obstruct flow through the catheter, but can break off to form a thromboembolism at any time. Animals with underlying diseases predisposing to hypercoagulability (e.g. endocrine disease, cardiac disease, severe inflammation) are considered to be at greater risk for thrombosis and/or thromboembolism. Identification of hypercoagulability is becoming easier due to the introduction of viscoelastic coagulation testing to veterinary practice (e.g. thromboelastography). In animals at risk of hypercoagulability, careful risk–benefit assessment should be performed before placement of a central catheter. Routine anticoagulation is not recommended in animals at risk of hypercoagulability with central venous catheters, but cannulated vessels should be evaluated frequently for thrombosis and catheters removed if there are any concerns.

Placement of a peripherally inserted central catheter via the saphenous vein may be preferred. Septicaemia is considered to be an absolute contraindication to central vein catheterization in human patients due to the increased risk of thrombophlebitis, although this contraindication is not considered absolute in small animal patients. Central lines are routinely placed in dogs and cats with sepsis.

Infection

Routine practice of good hygiene and aseptic techniques whenever intravenous catheters are placed and used, combined with daily catheter maintenance, are the best strategies for prevention of catheter-related infections. Catheter contamination will be minimized by limiting the number of disconnections from fluid lines and injection ports. The use of systemic antimicrobials does not reduce the risk of infection and is not recommended for prevention of infectious complications.

Dislodgement/catheter embolism

Embolism by a piece of an intravenous catheter is an uncommon but serious complication, which may result from inadvertent transection of the catheter with a blade or scissors as bandage or suture material is being removed. Extreme caution should be practised whenever sharp instruments are used near a catheter. If a catheter embolism occurs, however, the piece of catheter may be identifiable on radiographs if it is radiopaque. Depending on the site at which it lodges, it may be safe to leave it in place permanently, or retrieval may sometimes be possible using non-invasive intravascular techniques and fluoroscopy.

Air embolism

Air embolism may occur with any indwelling venous catheter. The risk of air embolism is thought to be greatest during the placement of central venous catheters. This can be avoided by delaying release of vascular occlusion until the catheter has been connected to the T-port. Air embolism can also occur if fluid administration sets are not flushed properly and air bubbles remain within the line. In most circumstances, when air embolism does occur, small emboli will be contained within the pulmonary vasculature without adverse clinical consequence.

Exsanguination

Blood loss may occur whenever a catheter becomes disconnected from its injection cap or fluid extension set. The risk of significant blood loss is greatest with arterial catheters as blood can be lost rapidly under arterial pressure. Animals with arterial catheters should always be under direct supervision. Animals with venous catheters can also suffer haemorrhage if the catheter becomes disconnected and a clot does not form; however, significant blood loss is rare. All animals with intravenous access should be observed at regular intervals.

Specialized techniques

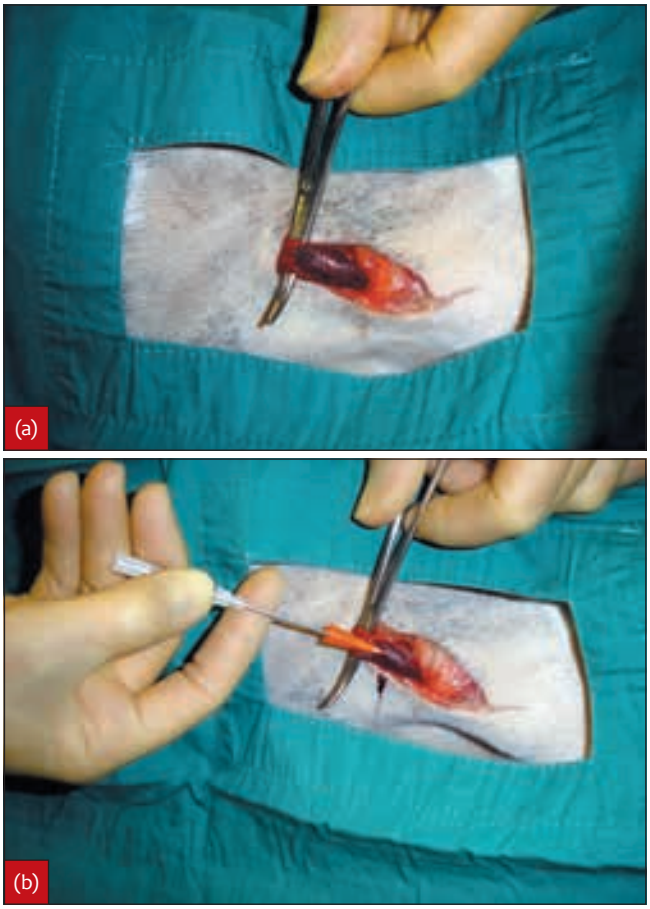
Cut-down technique for venous access

In some animals, it may not be possible to obtain percutaneous peripheral or central venous access and a surgical cut-down approach will be required. This occurs most commonly in animals with severe peripheral oedema or vascular collapse (hypovolaemia or shock). The technique may be used for peripheral or central veins and is similar for both. If time allows, strict aseptic technique should be followed; if not, clipping of the hair and brief wiping with an antiseptic solution will suffice. These catheters are considered to be ‘dirty’ and should be removed as soon as possible; they should never remain in place beyond 24 hours. Drainage of the site may be required after catheter removal.

After skin preparation, the location of the vein is identified using anatomical features and circumferential compression of the leg or compression of the neck using digital pressure at the thoracic inlet. The location of the

jugular vein can be estimated by drawing an imaginary line from the manubrium to the angle of the jaw. The jugular vein will be found approximately halfway along this line. The skin is pulled dorsally so that it no longer overlies the vein and a longitudinal incision is made through the skin to the subcutaneous tissues. The length of the incision will depend partially on the site and partially on the skill of the veterinary surgeon or nurse. The skin is allowed to return to the normal position, and the subcutaneous tissues are bluntly dissected away from the vein using the index fingers or sterile curved-tip haemostats. Catheter insertion is facilitated by removal of as much of the fascia from around the vein as possible (Figure 2.11).

Once the vein is exposed, catheter placement is accomplished using one of two techniques. The first technique utilizes two loops of suture material passed beneath the vein. The distal (for limbs) or cranial (for the jugular vein) loop is used to elevate and partially occlude the vein during placement, and the proximal (limb) or caudal (jugular vein) loop can subsequently be used to secure the catheter. This technique requires complete dissection of the vessel from the surrounding tissues. The other technique uses no suture; the catheter is placed in the conventional manner once the vein is directly visualized. Less dissection is required with this technique, although stabilization of the vessel is more challenging. Once the catheter is in place it should be secured immediately by suturing it to the vessel or surrounding tissues using absorbable suture material. The skin may then be sutured and the catheter bandaged into place as previously described.



2.11 An illustration of a cut-down technique. (a) The jugular vein is shown dissected free from the subcutaneous tissues. Stabilization of the vein with a pair of artery forceps or suture can aid subsequent catheter placement. (b) The catheter is placed into the vein, advanced and secured carefully before use.

Intraosseous catheters

Intraosseous access is particularly useful in cases where direct intravenous access is not possible but where rapid fluid administration is required, such as in hypovolaemic puppies or kittens, or in animals with severe vascular collapse. This route may be used to provide initial fluid resuscitation and medication until intravenous access is possible. Most substances that can be given intravenously may be given into the medullary space and absorption into the vasculature is extremely rapid. Although intraosseous needles are considered to access the central compartment, hypertonic and alkaline fluids may cause pain when infused and can lead to lameness. Intraosseous cannulas are commercially available (Figure 2.12); however, a spinal or bone marrow aspiration needle may be used. In neonates, a regular hypodermic needle may be used as the cortical bone is soft. Ideally, the needle should have a central stylet to prevent a core of bone from obstructing the needle. Automated devices for placement are available and provide a rapid way to access this compartment.



2.12 An example of an intraosseous cannula.

Placement of an intraosseous catheter is easy and rapid. The technique is described in Figure 2.13. Any site with a good marrow cavity may be used and suitable sites include:

- The medial aspect of the trochanteric fossa of the femur
- The flat medial surface of the proximal tibia, 1–2 cm distal to the tibial tuberosity
- The cranial aspect of the greater tubercle of the humerus
- The wing of the ilium.

The preferred sites are those in the femur and tibia. Damage to the sciatic nerve can be avoided by walking the needle off the medial edge of the greater trochanter. Damage to the growth plate is extremely unlikely in young animals with careful placement.

1. The skin overlying the chosen area is clipped and surgically prepared.
2. Local anaesthesia is infiltrated down to the level of the periosteum with 1% lidocaine.
3. A No. 11 blade is used to make a small skin nick.
4. The needle is inserted into the bone using a firm twisting motion until well seated through the cortex. When properly seated in the medullary cavity the needle will feel secure and movement of the needle will result in movement of the bone.
5. The needle should be flushed with heparinized saline and a T-connector or infusion set attached.
6. The cannula should be secured with either sutures or tape and the entry site covered with a sterile swab and antiseptic ointment. A bulky wrap should be applied to prevent damage to the needle.

2.13 Placement of an intraosseous cannula.

Once in place, fluids can be given rapidly to provide volume resuscitation and, despite concerns about hypertonicity, dextrose is often given successfully to collapsed neonates by this route. Intraosseous catheters and needles may be left in place but are difficult to secure in active animals; their most useful application is therefore during initial stabilization where intravenous access is impossible. Extravasation may occur so the subcutaneous tissues should be monitored. Should this occur, the cannula should be removed and a different bone selected for subsequent placement, or efforts made to place an intravenous catheter once initial resuscitation has been performed.

Arterial catheterization

Arterial catheters are placed less commonly than venous catheters in veterinary practice. They are particularly useful for monitoring critically ill patients as they allow direct arterial blood pressure measurement and serial collection of arterial blood gas samples. They require greater technical skill to place than venous catheters; however, with practice arterial catheters may be placed in the majority of medium- to large-sized dogs. Placement in cats and small dogs is more challenging.

The main sites used for arterial catheterization are the dorsal pedal artery, femoral artery, auricular artery, coccygeal artery and palmar metacarpal artery. A 20–22 G peripheral venous catheter can be placed in most arteries. The site is prepared gently with an antimicrobial solution and surgical spirit. Vigorous scrubbing may cause arterial spasm and should be avoided. Use of a small stab incision (No. 11 blade) through the skin facilitates placement as it minimizes damage to the catheter tip. The artery is palpated during placement and this is used to guide the catheter tip towards the vessel (Figure 2.14). As the walls of arteries are more muscular than those of veins, entrance of the catheter into the vessel is aided by short, firm, purposeful movements once the catheter tip is in the region of the artery. The flash chamber is watched closely for signs of vessel penetration, and once this has occurred the stylet may need to be flattened and advanced another millimetre or two into the vessel before the catheter is advanced into place. To facilitate feeding of the catheter, it is important that the catheter is aligned parallel to the artery at all times and approached at a gentle angle (10–30 degrees). The dorsal pedal artery sits between the fourth and fifth metatarsal bones, then runs across the cranial tarsus at about 30 degrees to the long axis of the limb from medial to lateral. Ideally, the artery should be penetrated as low down as possible, in order to minimize compression of the catheter when the tarsus is flexed. Once in place, the catheter is secured firmly, bandaged and heparinized. It may then be used as required for blood pressure monitoring and collection of samples for blood gas analysis.



2.14 Placement of an arterial catheter in the dorsal pedal artery. The artery is palpated during insertion and the catheter is aligned with the artery to facilitate feeding.

Arterial catheters may be placed in animals that are thrombocytopenic or coagulopathic, but this should be done with care and only the more distal sites on the limb should be used where pressure can be applied. There is an increased risk of bleeding in these situations; if this occurs firm pressure should be applied to the site for 10–15 minutes. Arterial catheters should be maintained in a similar way to venous catheters; however, they require more frequent flushing (at least every 1–2 hours) as they are prone to occlusion. Alternatively, arterial catheters used for continuous monitoring of direct arterial blood pressure may be connected to a disposable pressure transducer, through which dilute heparinized saline is continuously infused under pressure via microtubing (Figure 2.15). Care must be taken to identify clearly arterial catheters as such, to avoid inadvertent administration of fluids or drugs into the artery. Due to the risk of vascular damage and subsequent tissue necrosis, use of arterial catheters should be restricted to blood sampling and pressure monitoring; they should never be used for the administration of drugs or fluids.



2.15 Constant flushing of an artery via microtubing.

The pulmonary artery catheter

Cardiac catheterization is an uncommon procedure generally reserved for the intensive care unit and which requires the participation of an experienced specialist. Pulmonary artery (PA) catheters (Swann–Ganz catheters) are specialized multi-lumen catheters equipped with a balloon-tip to facilitate catheterization of the pulmonary artery and subsequent measurement of vascular pressures (wedge pressure). They are also equipped with a thermistor to allow

determination of cardiac output and systemic vascular resistance. Select PA catheters may also allow additional monitoring (e.g. oximetry). Indications for the use of a PA catheter include animals that are refractory to routine fluid resuscitation, animals with known cardiac disease that require aggressive fluid therapy and animals with distributive shock. Contraindications for cardiac catheterization include: the presence of bleeding disorders, acquired coagulopathies or severe hypercoagulability; unstable cardiac conditions; and any pre-existing risk for complications (i.e. severe dysrhythmias or predisposition to them). These catheters are rarely placed in veterinary practice.

References and further reading

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White R (2002) Vascular access techniques in the dog and cat. *In Practice* **24**, 174–192

Useful websites

A number of companies provide intravenous catheters and other supplies such as connectors and needle-free devices. The following is a list of those that the author has found useful:

Arrow International:
www.arrowintl.com

Infusion Concepts:
www.infusionconcepts.com

MILA International:
www.milainternational.com

Smiths Medical:
www.smiths-medical.com/uk

Terumo:
www.terumomedical.com

Vygon:
www.vygon.co.uk

Chapter 3

Assessment and treatment of shock

Emily Thomas and Elise Boller

Shock is broadly defined as an imbalance between oxygen delivery to tissues (DO_2) and oxygen consumption by tissues (VO_2), resulting in impaired cellular metabolism and energy production. In rare cases, disruption of cellular metabolism may result in deranged oxygen consumption such that shock exists despite normal DO_2 (e.g. mitochondrial dysfunction due to cyanide toxicity or sepsis). The effects of shock are seen at the cellular, tissue and ultimately organ levels, and may cause significant morbidity and mortality without prompt, aggressive treatment.

Shock may be classified according to its underlying aetiological, haemodynamic or functional effects. In veterinary medicine, a commonly used haemodynamic classification includes hypovolaemic, cardiogenic, obstructive and distributive types of shock. Importantly, multiple types of shock can coexist within one patient; for example, hypovolaemic and obstructive shock (a patient with gastric dilatation–volvulus (GDV)), or hypovolaemic and distributive shock (a patient with septic peritonitis). Additionally, several clinical stages of shock are recognized, and are characterized based on the extent of physiological compensation. The effects of shock are initially reversible, but become irreversible in the late clinical stages.

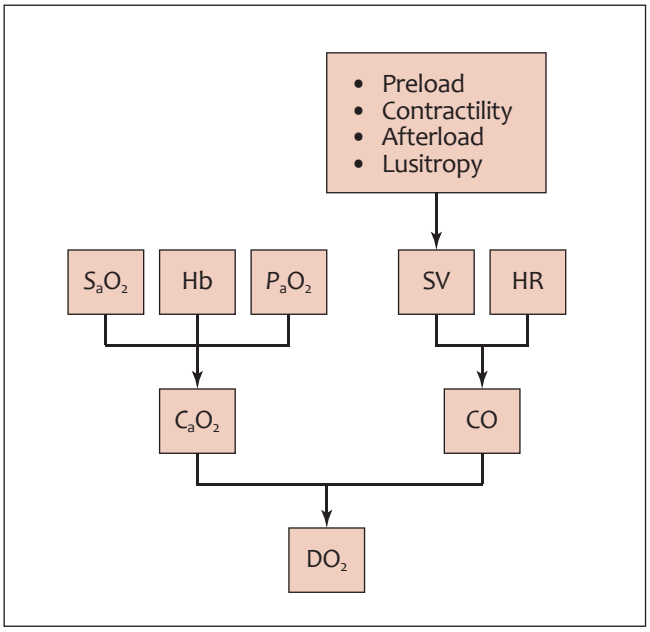
Treatment varies according to the type of shock. The most commonly seen in small animal practice is hypovolaemic shock, for which the initial treatment is fluid resuscitation. However, it is important to determine the cause of shock and to treat accordingly, as treatment may vary depending on the underlying aetiology. For example, fluid resuscitation may be detrimental for patients in some types of cardiogenic shock (e.g. those with respiratory compromise along with pump failure), and some animals in distributive shock may not respond appropriately to fluid therapy and will require treatment with vasopressors.

The prognosis for shock is variable, from good to grave depending on the underlying cause and clinical stage. However, even patients presenting with dramatic clinical signs may respond well to appropriate treatment, and these cases can be very rewarding to treat.

Pathophysiology

An imbalance between oxygen delivery and oxygen consumption

Oxygen delivery (DO_2) is determined by cardiac output (the volume of blood pumped by the heart each minute), haemoglobin concentration, arterial oxygen saturation and, to a small extent, arterial partial pressure of oxygen (Figures 3.1 and 3.2). Under normal physiological conditions, DO_2 greatly exceeds VO_2, and only 20–30% of delivered oxygen is extracted for consumption. Typically in shock states, either DO_2 is decreased and/or VO_2 is increased, which ultimately leads to anaerobic metabolism and therefore decreased cellular energy production. In very rare circumstances there is a primary defect in mitochondrial metabolism that decreases the ability of the cells to utilize oxygen to produce energy (decreased VO_2). Multiple factors may alter the balance between DO_2 and VO_2 (Figure 3.3).



3.1 Components that determine delivery of oxygen. C_aO_2 = blood oxygen content; CO = cardiac output; DO_2 = oxygen delivery; Hb = haemoglobin; HR = heart rate; P_aO_2 = arterial partial pressure of oxygen; S_aO_2 = arterial oxygen saturation; SV = stroke volume.

$$DO_2 = CO \times C_aO_2$$
$$CO = HR \times SV$$
$$C_aO_2 = (1.34 \times [Hb] \times S_aO_2) + (0.003 \times P_aO_2)$$

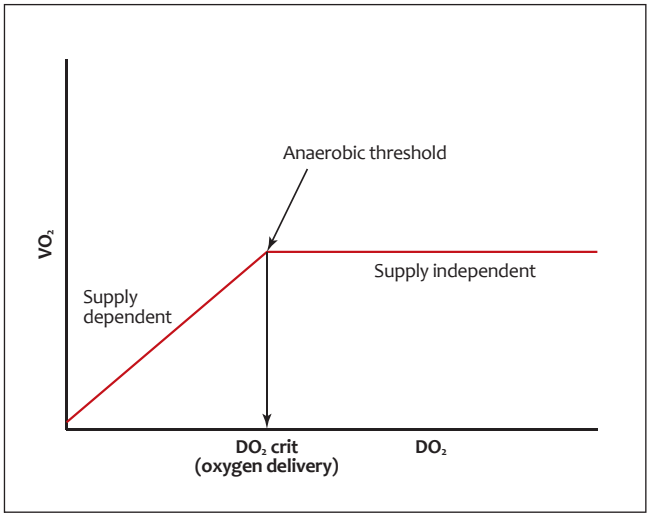
3.2 Equations for determination of oxygen delivery. C_aO_2 = blood oxygen content; CO = cardiac output; DO_2 = oxygen delivery; Hb = haemoglobin; HR = heart rate; P_aO_2 = arterial partial pressure of oxygen; S_aO_2 = arterial oxygen saturation; SV = stroke volume.

Example factors	DO_2	VO_2
Hypovolaemia; anaemia; hypoxaemia; maldistribution of blood flow caused by vasodilatation	Decreased	Normal
Status epilepticus; fever; excessive work of breathing	Normal	Increased
Mitochondrial dysfunction, e.g. sepsis, cyanide toxicity	Normal	Decreased

3.3 Alterations in the relationship between oxygen delivery (DO_2) and oxygen consumption (VO_2) in response to different factors. The altered relationship can result in shock states and decreased cellular energy production. Note that some disease processes, such as sepsis, may affect multiple factors.

As DO_2 decreases, the cellular oxygen extraction ratio increases in most tissues, enabling VO_2 to remain constant. However, this physiological reserve is exhausted once the oxygen extraction ratio is maximized. The DO_2 level at which this occurs is known as the 'critical DO_2'. Below this critical level, VO_2 starts to reduce linearly with DO_2 (a state known as 'supply dependency'), resulting in a switch from aerobic to anaerobic metabolism (Figure 3.4). Alternatively, a switch to anaerobic metabolism can result from increased tissue oxygen consumption, as seen with status epilepticus, fever or increased work of breathing. Finally, disease processes such as sepsis may cause a primary impairment of oxygen utilization at the mitochondrial level, resulting in decreased VO_2. In these instances, anaerobic metabolism occurs at higher DO_2 levels than usual.

When cells convert to anaerobic metabolism, cellular energy production is greatly decreased. Under aerobic conditions each molecule of glucose yields 38 molecules of adenosine triphosphate (ATP), whereas under anaerobic conditions, only two ATP molecules are produced and lactate and free hydrogen ions are formed as byproducts. Normal cellular processes are affected both by energy depletion and by intracellular acidosis, leading to changes in cell membrane permeability and alterations in intracellular ion ratios, which may ultimately cause cell dysfunction and death.



3.4 The normal relationship between oxygen delivery (DO_2) and oxygen consumption (VO_2). When DO_2 falls below the critical level (DO_2 crit) anaerobic metabolism ensues, and VO_2 becomes dependent on DO_2.

Organ dysfunction and ischaemia-reperfusion injury

The changes in cellular metabolism result in complicated injury to tissues and organs secondary to ischaemia, inflammation and apoptotic signalling, among other pathological changes. This is exacerbated by the systemic release of inflammatory cytokines such as tumour necrosis factor-α (TNF-α), interleukin-1 (IL-1) and IL-8. Clinical signs of organ dysfunction secondary to shock may vary by species; the gastrointestinal system is commonly referred to as the 'shock organ' in dogs, whereas lung injury seems to be common in cats. In dogs, the splanchnic circulation is one of the first to be compromised because blood is diverted to vital organs such as the heart and brain, which normally have a high oxygen extraction ratio and little physiological reserve. Organ injury may remain subclinical and/or localized, but as shock progresses, multiple organ dysfunction syndrome (MODS) may ensue (Figure 3.5).

Although there is no consensus definition for MODS in veterinary patients, a working definition is dysfunction of two or more organs in critically ill patients such that organ system-specific supportive care is required to maintain

Organ system	Clinical signs of dysfunction	Diagnostic test abnormalities
Renal	Abnormal urine output; peripheral and pulmonary oedema; weight gain	Elevated serum urea, creatinine, phosphate, potassium; isosthenuria; metabolic acidosis
Cardiac and vascular	Worsening clinical signs of hypoperfusion despite adequate fluid therapy; oedema; weight gain; persistent hypotension; irregular heart rate with pulse deficits	Decreased ejection fraction on echocardiography; arrhythmias; hypoalbuminaemia
Respiratory	Increased respiratory rate/effort; pulmonary crackles; cyanosis	Low S_pO_2, P_aO_2; alveolar infiltrates evident on thoracic radiographs
Hepatic	Icterus; encephalopathy; diarrhoea; gastrointestinal bleeding	Increased serum liver enzyme activity; elevated serum total bilirubin; elevated ammonia and bile acids
Gastrointestinal	Diarrhoea; melaena; vomiting; regurgitation; ileus; intolerance to feeding; decreased gut sounds	Elevated serum BUN; abnormal abdominal ultrasonography; abnormal auscultation
Nervous	Dull or dull mentation; peripheral neuropathy; seizures	Abnormal neurological examination
Coagulation	Thrombosis or bleeding	Prolonged PTT, PT; elevated D-dimers and/or FDPs; thrombocytopenia
Endocrine	Poor vascular responsiveness (CIRCI); relative insulin resistance	Low basal cortisol/delta-cortisol; hyperglycaemia

3.5 Overview of common clinical signs and diagnostic test abnormalities found with multiple organ dysfunction syndrome (MODS). Diagnosis and management of individual organ system dysfunction is discussed in more detail in the relevant chapters. BUN = blood urea nitrogen; CIRCI = critical illness-related corticosteroid insufficiency; FDP = fibrin degeneration product; P_aO_2 = arterial partial pressure of oxygen; PT = prothrombin time; PTT = partial thromboplastin time; S_pO_2 = peripheral capillary oxygen saturation.

adequate homeostasis (Johnson *et al*., 2004; Hackett, 2011). Since MODS reflects a systemic response to shock, dysfunction of any organ may occur, including those distant from the original underlying injury. Patients that develop MODS have increased mortality, and its early recognition and prompt treatment are essential (Kenney *et al*., 2010).

Unfortunately, pathophysiological changes continue even after tissue perfusion is restored. As oxygen is restored to damaged cells, reperfusion injury may occur. Under ischaemic conditions there is build-up of xanthine oxidase within cells. This reacts with oxygen to produce reactive oxygen species (ROS), which result in local oxidative damage, cell death and tissue injury. ROS may also enter the systemic circulation and cause more widespread oxidative damage.

Classification of shock

Various classification schemes for shock have been proposed and there is no single 'correct' system. In this chapter shock states are classified according to approach to treatment, and therefore broadly as 'circulatory' or 'non-circulatory.'

- Circulatory types of shock (hypovolaemic, cardiogenic, obstructive, distributive) all result in tissue hypoperfusion (reduced DO_2) and, with the exception of cardiogenic shock, usually require treatment with intravenous fluids.
- Non-circulatory types of shock (hypoxic, metabolic) arise when other factors affect the balance between DO_2 and VO_2; treatment of non-circulatory forms of shock varies depending on the underlying aetiology.

Whilst classification schemes are clinically helpful, any scheme is necessarily a vast oversimplification of the complex pathophysiology described above. Thus, patients often present in shock that may be classified concurrently into several categories. For example, a dog with GDV may be in hypovolaemic, cardiogenic and obstructive shock all at the same time. Figure 3.6 summarizes the shock classification scheme with the definitions used in this chapter.

Broad category	Type of shock	Definition
Circulatory	Hypovolaemic	Decreased intravascular volume
	Cardiogenic	Reduced cardiac output ('forward' or 'pump' failure)
	Obstructive	Physical obstruction to blood flow leading, ultimately, to reduced filling of the left side of the heart (heart and/or great vessels)
	Distributive	Maldistribution of blood flow (vasodilatation, vasoconstriction)
Non-circulatory	Hypoxic	Decreased oxygen content in arterial blood (anaemia, hypoxaemia, dyshaemoglobinaemia)
	Metabolic	Impaired cellular metabolism

3.6 Shock classification scheme.

Circulatory types of shock

Hypovolaemic shock

Hypovolaemic shock is defined as shock resulting from a decrease in blood volume, and is the most common form of shock seen in small animal practice. It may occur with volume loss due to haemorrhage (internal or external), with loss of other body fluids (e.g. vomiting, diarrhoea, polyuria, third-spacing of fluids) or due to decreased intake (e.g. restricted access to food and/or water) (Figure 3.7).

In clinical practice, the term 'hypovolaemia' is used to refer to a fluid deficit in the intravascular space, while the term 'dehydration' is used to refer to a deficit in the interstitial space. It is very important to make a clinical distinction between a patient that demonstrates interstitial dehydration and one that is hypovolaemic; hypovolaemia is life-threatening and must be treated immediately with acute resuscitative fluid therapy, while interstitial dehydration is not and can be corrected more slowly, over 6–24 hours.

Fluid loss		
Haemorrhagic	Internal	Cavitary: peritoneal, retroperitoneal, pleural or pericardial spaces
		Non-cavitary: gastrointestinal, urinary, subcutaneous, bleeding into tumours
	External	Trauma
Non-haemorrhagic	Internal	Cavitary: peritoneal, retroperitoneal, pleural or pericardial spaces
		Non-cavitary: interstitial space, urinary tract, gastrointestinal tract
	External	Urine, vomitus, diarrhoea, excessive salivation, wounds, burns
Decreased fluid intake		
Unable to drink	Restricted access to water Problems with prehension and swallowing Vomiting or regurgitation	
Uninterested in drinking	Neurological disorders	

3.7 Causes of hypovolaemic shock.

Distributive shock

Distributive shock is defined as a maldistribution of blood flow, most commonly inappropriate vasodilatation due to sepsis or the systemic inflammatory response syndrome (SIRS). It is clinically distinct from other forms of shock in that it initially results in a hyperdynamic state, which in dogs is characterized by increased cardiac output and peripheral vasodilatation (see below). Release of inflammatory mediators and induction of the nitric oxide pathway causes inappropriate vasodilatation such that the vascular volume that needs to be filled is increased, which leads to maldistribution of blood flow and a decrease in effective circulating volume such that DO_2 to the tissues is compromised. As distributive shock worsens it usually progresses from a hyper- to hypodynamic state.

SIRS is systemic inflammation resulting from infectious or non-infectious causes. Non-infectious SIRS may be caused by insults such as trauma, pancreatitis, shock, surgery or burns. Its strict definition is the presence of two or more defined criteria in an animal with an inflammatory focus (Figure 3.8). These criteria are very non-specific (many healthy patients will fulfil them after exercise or during the stress of clinical examination) but the definition

Parameter	Dogs	Cats
Heart rate (beats per minute)	>120	<140 or >225
Respiratory rate (breaths per minute)	>40	>40
Temperature (°C)	<38.1 or >39.2	<37.8 or >40
White blood cells/μl	<6000 or >16,000	<5000 or >19,000
Band neutrophils (%)	>3	

3.8 Criteria for the diagnosis of systemic inflammatory response syndrome (SIRS). In addition to the presence of an inflammatory focus, two or more criteria must be present in dogs for diagnosis, and three or more in cats.
(Hauptman *et al.*, 1997; Brady *et al.*, 2000)

remains useful for those patients where inflammation is clinically suspected, especially in patients that appear to be clinically ill.

Veterinary definitions of sepsis and septic shock are not universally agreed upon but a good working definition of sepsis is the clinical syndrome of systemic inflammation associated with infection. It represents a dysregulation of host response to infection and is life threatening. Infection may be of bacterial, viral, fungal or protozoal origin. In humans, the term 'severe sepsis' has been discarded and replaced by the term 'sepsis' because sepsis is, by definition, a severe and life-threatening condition. Septic shock is sepsis accompanied by organ dysfunction, such as arterial hypotension despite volume resuscitation, or other cellular/metabolic abnormalities that substantially increase mortality. There is no current consensus on definitions in veterinary medicine. Importantly, it is not only the infection itself that causes the morbidity associated with sepsis, but also the host response to the infection. Dysregulation of vasomotor tone, coagulation and endothelial permeability are all hallmarks of the sepsis/SIRS syndrome.

Obstructive shock

Obstructive shock results from physical obstruction to blood flow, either to or from the heart, or through the great vessels. It shares many characteristics with cardiogenic shock and is often categorized together with cardiogenic shock rather than in its own distinct category. Causes of obstructive shock include GDV, pericardial tamponade, tension pneumothorax, and pulmonary or aortic thromboembolism.

Cardiogenic shock

There is often confusion about the term 'cardiogenic shock'. In its purest sense, cardiogenic shock occurs when cardiac output is reduced (i.e. 'forward' or 'pump' failure). Cardiac output is a product of stroke volume and heart rate. Systolic and diastolic dysfunction and cardiac arrhythmias may cause decreased stroke volume and/or abnormal heart rates. Common causes of cardiogenic shock, grouped according to their effect on cardiac function, are summarized in Figure 3.9. It is important to note that not all patients in congestive heart failure (build-up of fluid 'behind' the heart or 'backward' failure) are in cardiogenic shock, while most animals in cardiogenic shock will concurrently be in congestive heart failure.

Patients with chronic cardiomyopathies develop compensatory mechanisms such as cardiac dilatation and increased heart rate to cope with a gradual decline in cardiac output; however, as the disease progresses and compensatory mechanisms fail or an arrhythmia develops, the patient may show overt clinical signs of forward failure. Complicating factors, such as the onset of backward congestive heart failure (cardiogenic pulmonary oedema, which causes hypoxic shock), may confound the clinical picture. The prognosis is typically guarded for patients in cardiogenic shock, except when it is caused by a reversible underlying disease such as sepsis-induced myocardial dysfunction.

Cardiogenic shock is typically not treated with intravenous fluids, but rather with medications directed at increasing cardiac output (inotropes and anti-arrhythmic drugs).

Non-circulatory types of shock

Hypoxic shock

Hypoxic shock is defined as shock resulting from decreased oxygen content in arterial blood (C_aO_2). Hypoxic shock may arise due to decreased haemoglobin or dysfunctional haemoglobin as in dyshaemoglobinaemias, or

Parameter	Dysfunction	Cause	Examples
Stroke volume	Systolic dysfunction	Decreased cardiac contractility	• Dilated cardiomyopathy • Sepsis • Endomyocarditis • Myocardial infarction • End-stage mitral valve endocardiosis
		Reduced 'forward' flow	• Hypertrophic obstructive cardiomyopathy • Aortic stenosis • Chordae tendinae rupture
	Diastolic dysfunction	Inability of ventricular muscle to relax	• Hypertrophic cardiomyopathy
		Physical restriction	• Pericardial tamponade
		Reduced filling time	• Tachyarrhythmias
		Reduced filling pressure	• Severe hypovolaemia
Heart rate	Bradyarrhythmias	Conduction disturbances	• Third-degree atrioventricular (AV) block • High-grade second-degree AV block • Atrial standstill • Sick sinus syndrome
	Tachyarrhythmias	Conduction disturbances	• Supraventricular tachycardia • Ventricular tachycardia

3.9 Causes and types of cardiogenic shock.

desaturated haemoglobin caused by decreased partial pressure of oxygen (see Figures 3.1 and 3.2). Decreased C_aO_2 acts to decrease DO_2, sometimes despite normal tissue perfusion, resulting in hypoxic shock. The most common cause of hypoxic shock in clinical veterinary practice is severe anaemia, which is not necessarily associated with hypovolaemia (e.g. immune-mediated haemolytic anaemia). It is important to note that in these cases, low C_aO_2 arises directly from low levels of haemoglobin, not from respiratory disease, and diagnostic tests such as pulse oximetry and arterial blood gas analysis may be unremarkable.

Severe pulmonary disease is, however, a separate potential cause of hypoxic shock, and is not uncommon. For example, severe aspiration pneumonia or pulmonary contusions may reduce oxygen uptake sufficiently to cause hypoxic shock.

Finally, and uncommonly, alterations in the binding affinity of haemoglobin for oxygen may result in hypoxaemia despite normal haemoglobin levels. Examples include carbon monoxide poisoning (carboxyhaemoglobinaemia) and paracetamol (acetaminophen) toxicosis (methaemoglobinaemia).

Metabolic shock

Metabolic shock results when cellular aerobic metabolism is reduced despite normal DO_2. Severe metabolic derangements such as hypoglycaemia, acidaemia and primary mitochondrial dysfunction can result in metabolic shock; however, many patients with these conditions will concurrently have other types of shock. Normal aerobic metabolism relies on sufficient substrate (glucose) entering the cell, followed by oxidative phosphorylation within the mitochondria. Severe hypoglycaemia can therefore result in metabolic shock, as can disorders affecting any stage of mitochondrial respiration. Sepsis is thought to cause an intrinsic derangement in mitochondrial respiration known as 'cytopathic hypoxia'. Cyanide toxicity, although rarely seen, inhibits oxidative phosphorylation by binding to cytochrome oxidase within the mitochondria. Both these disorders inhibit aerobic metabolism and may result in metabolic shock.

Diagnosis

Physical examination and physiological response to shock

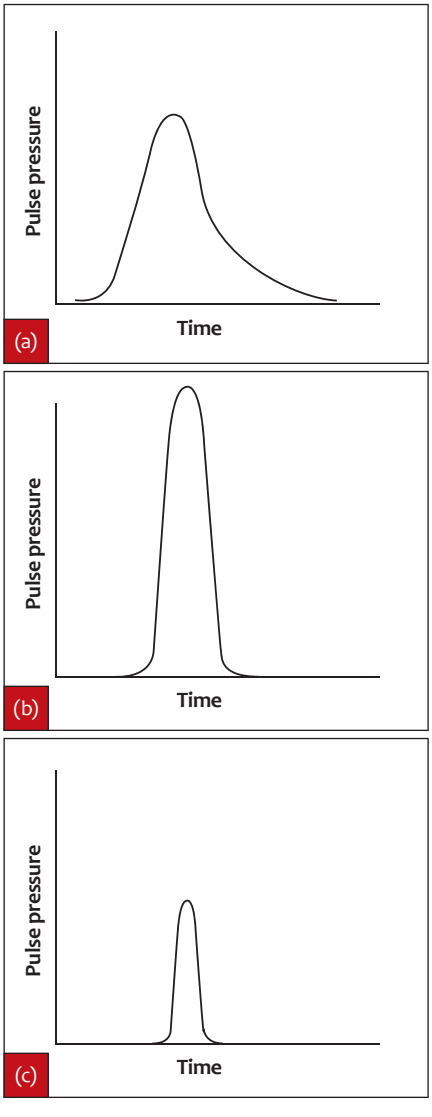
Rapid recognition of shock is essential and a brief history and triage examination should be sufficient for initial diagnosis. The major body systems should be examined during triage, with particular attention paid to the cardiovascular system (heart rate, cardiac auscultation, mucous membrane colour, capillary refill time (CRT), and pulse synchrony and quality), respiratory system (respiratory rate, effort, pattern, mucous membrane colour, respiratory auscultation) and neurological system (mentation and gait) (see Chapter 1). Clinical signs of shock may affect all these body systems and vary according to the type and stage of shock. There is also species variation, with cats showing different signs from dogs (Figure 3.10).

In early shock, clinical signs in dogs reflect a compensated state and may easily be overlooked. The canine patient may be ambulatory and alert, often not yet showing pronounced mentation changes. There may be a mild increase in heart rate and respiratory rate, hyperaemic

Parameter	Dogs	Cats
Heart rate	Tachycardia	Bradycardia
Mucous membrane colour	Hyperaemic	Pale
Capillary refill time	<1 second	Variable
Temperature	Often high	Usually low

3.10 Typical clinical signs of distributive shock in dogs and cats.

mucous membranes, and a shortened CRT of <1 second. The pulse quality may be normal or tall and narrow (Figure 3.11). As hypovolaemic or cardiogenic shock progresses, the mucous membranes soon become pale due to vasoconstriction. The clinical signs of this compensatory state can be explained by a predictable neurohormonal response to decreased effective circulating volume that is aimed at preserving cardiac output: catecholamine release results in increased heart rate, contractility and peripheral vasoconstriction. Decreased renal blood flow resulting from low cardiac output also activates the renin–angiotensin–aldosterone system. This increases sodium and water retention by the kidneys in an attempt to prevent further decreases in blood volume, and further promotes vasoconstriction. Other water-retaining mechanisms such as antidiuretic hormone release may also come into play.



3.11 Pulse pressure profiles. Assessing the height and width of the pulse together allows an estimation of pulse volume. (a) Normal palpable pulse pressure profile. (b) Hyperdynamic pulse (tall and narrow) as palpated in compensated hypovolaemia. (c) Weak pulse (short and narrow) as palpated in decompensated hypovolaemia.

As shock and hypoperfusion progress, dogs become overtly tachycardic and tachypnoeic, with pale mucous membranes (Figure 3.12a), a prolonged CRT (>1.5–2 seconds) and decreased pulse pressure. Mentation may be depressed, and the skin and extremities are often cold to the touch, as blood flow is diverted to the central organs. Rectal temperature may decrease. In the terminal stages patients become progressively bradycardic, CRT is difficult to detect, peripheral pulses are weak or absent, the animal is hypothermic, stuporous or comatose, and oliguria or anuria may be present. This stage of shock is often irreversible despite aggressive attempts at resuscitation. These advanced clinical signs are explained by progressive failure of neurohormonal responses to adequately compensate for the worsening hypoperfusion; it is not uncommon for veterinary patients to be presented in this decompensated stage of shock.

Dogs with distributive shock share the initial hyperdynamic clinical signs seen in other types of compensated shock. However, instead of progressing to vasoconstriction and pale mucous membranes, the patient remains hyperaemic (Figure 3.12b) with a brisk CRT (<1 second) even in the more advanced stages of shock, due to vasomotor dysfunction resulting in inappropriate vasodilatation. In the very late stages, CRT will become prolonged.

Cats are assessed for clinical signs of shock in the same manner as dogs; however, the clinical signs differ in several ways. First, although the heart rate may increase in cats, heart rates in this species are typically not as proportionately elevated as in dogs. In fact, having a lower than expected (or indeed lower than normal) heart rate may be a sign of shock in cats, particularly in septic cats. Second, their mucous membranes are normally paler than dogs, so appreciating paleness as a sign of shock can be challenging in cats. Third, evaluating the pulse quality and profile in cats is challenging normally and even more so in cats with shock. Cats tend to be quiet patients, so assessing a cat for the hallmark signs of shock (quiet, weak, dull mentation) may also be challenging. Finally, cats do not always have fever with sepsis; in fact they are commonly hypothermic. For all of these reasons, identifying shock in cats can be more challenging. It is therefore important to use all available tools, subjective and objective, to confirm a clinical suspicion that a cat is in shock. Monitoring tools such as blood pressure and lactate measurement can be useful in this regard.

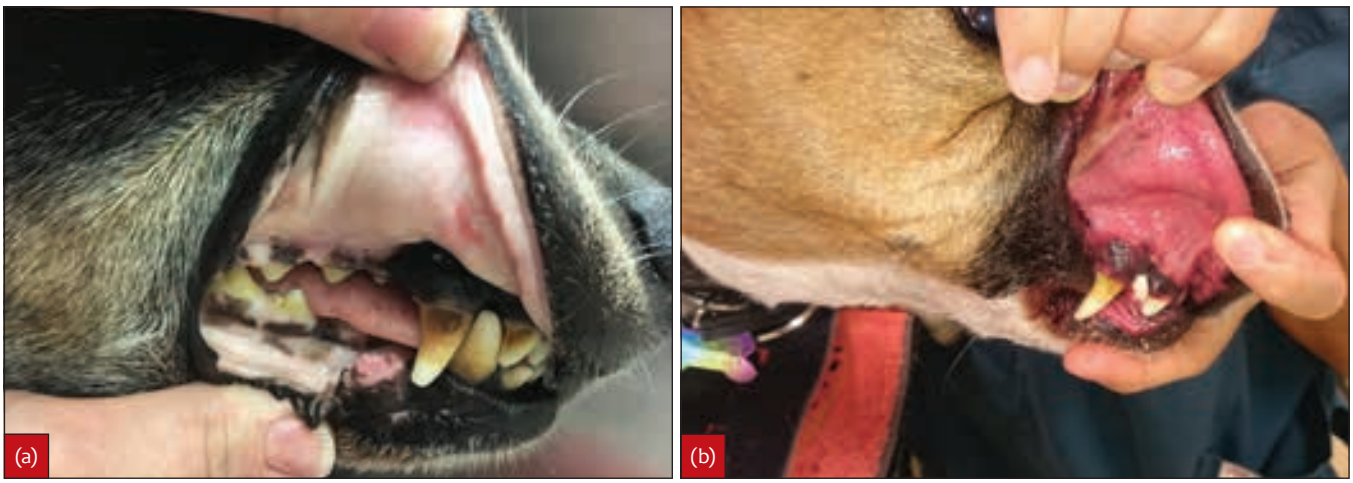
If cardiogenic shock is present then clinical signs consistent with cardiac abnormalities are often, but not always, detected on physical examination. Signs may include auscultation of a heart murmur, gallop rhythm or arrhythmia, with or without pulse deficits. If there is concurrent congestive (backward) heart failure, increased respiratory rate and effort with either crackles (pulmonary oedema) or dull lung sounds (pleural effusion) on pulmonary auscultation may be noted. Jugular distension/pulses and ascites may be evident with right-sided backward failure.

Shock is a very dynamic state and a patient's clinical status may change rapidly. The importance of repeating the physical examination during and after initial stabilization, and at frequent intervals during hospitalization, cannot be overemphasized. Assessment of the major body systems should typically be repeated every 15–30 minutes during initial stabilization and at least every 4 hours after that until the patient is deemed fully stable. Some patients may require more frequent monitoring than this.

Diagnostic tests

Shock is primarily a clinical diagnosis. Resuscitative treatment should be prioritized over extensive diagnostic testing in unstable patients. Most routinely performed tests in shock patients are used to determine the underlying cause of shock, assess organ damage and guide therapy, rather than to diagnose shock per se. A broad general approach to initial diagnostic testing for a patient in shock is outlined in Figure 3.13, although this will need to be tailored for individual patients. Almost all the suggested tests can be performed while resuscitative treatment is under way.

The authors' general approach is to place an intravenous catheter and, if possible, draw blood samples from the intravenous catheter for an initial emergency database (see Chapter 1), serum biochemistry and haemogram (and possibly a coagulogram or blood typing as required). Acute resuscitative fluid therapy (if appropriate to the type of shock present) is then commenced. The collection of blood samples should never significantly delay initiation of resuscitative measures. Other diagnostic tests such as imaging are usually delayed until the patient is more stable.



3.12 Assessment of mucous membrane colour in hypovolaemic *versus* distributive shock. (a) Hypovolaemia causes mucous membrane pallor with a prolonged capillary refill time (CRT). (b) Maldistribution of blood flow causes hyperaemic mucous membranes with a brisk CRT in distributive shock.

All patients

- Major body system assessment and full physical examination
- Placement of ECG leads for monitoring heart rate and rhythm
- Non-invasive arterial blood pressure measurement
- S_pO_2 measurement
- Blood sampling from the intravenous catheter at placement:
  - Blood from the hub of the catheter can be used to run an emergency database (PCV, TS, blood glucose, BUN, blood smear; see Chapter 1)
  - Where it is possible to collect further blood samples at placement without compromising the catheter, consider:
    - Cage-side venous blood gas, electrolyte, lactate measurement (typically only 0.1–0.2 ml of blood required)
    - Filling a serum gel and EDTA blood tube and reserving for later haematology and biochemistry panels

Selected patients

- 3-lead ECG measurement in patients with tachycardia, bradycardia or a suspected arrhythmia
- Ultrasound examination of the abdomen and/or pleural and pericardial spaces for free fluid (Point-of-care ultrasound scan (POCUS); see Chapters 1 and 24) in patients in which fluid accumulation is suspected based on clinical history, examination or results of the emergency database (e.g. low PCV/TS with no evidence of external haemorrhage)
- Diagnostic abdominocentesis, thoracocentesis or pericardiocentesis if required (thoracocentesis and pericardiocentesis may also be therapeutic)
- Radiography is almost always delayed until after initial stabilization, with rare exceptions (e.g. GDV) where a rapid radiographic diagnosis is required
- Blood collection for blood typing if anaemia is suspected, or coagulation panel if a coagulopathy is suspected

3.13 General approach to basic diagnostic testing for patients in shock. Resuscitative treatment should be prioritized over testing, and particular care should be taken with dyspnoeic animals whose condition may be worsened by the stress of handling.
BUN = blood urea nitrogen; ECG = electrocardiogram; EDTA = ethylenediaminetetraacetic acid; GDV = gastric dilatation–volvulus; PCV = packed cell volume; S_pO_2 = peripheral capillary oxygen saturation; TS = total solids.

Lactate

Lactate is produced as a byproduct of anaerobic metabolism and therefore increases in shock states. Multiple veterinary experimental and clinical studies have shown that both arterial and venous lactate concentrations increase with shock (type A hyperlactataemia). Initial lactate levels have been correlated with survival and used to predict outcome in veterinary patients, although more recently interest has focused on serial lactate measurement and assessment of lactate clearance as a prognostic tool (see Monitoring shock resuscitation below). In one study of dogs requiring intravenous fluid therapy, those with lactate concentrations higher than the reference interval 6 hours after presentation were more likely to die (Stevenson *et al.*, 2007).

Measurement of lactate should be considered part of an initial database in emergency patients; it can be quickly and reliably measured using handheld lactate meters and many blood gas analysers include lactate measurement. The required sample size is often only one drop of blood. Reference ranges vary, but a value >2.5 mmol/l is generally considered elevated. Whilst the most common cause of hyperlactataemia is shock, other disease processes may sometimes result in elevated lactate in the absence of shock (type B hyperlactataemia) due to failure of lactate clearance or causes of anaerobic metabolism that are not related to perfusion. Examples include renal failure, hepatic dysfunction and neoplasia (Figure 3.14).

Type of hyperlactataemia	Underlying cause	Prevalence
A: tissue hypoxia present	Decreased DO_2 Increased VO_2	Common
B: tissue hypoxia absent	B1: underlying disease causing decreased lactate clearance Examples: acute hepatitis, chronic kidney disease, hyperthyroidism, diabetes mellitus, neoplasia, sepsis/SIRS	Uncommon
	B2: toxins inhibiting oxidative phosphorylation Examples: paracetamol, salicylates, ethylene glycol, carbon monoxide, cyanide, strychnine, terbutaline, nitroprusside, halothane, activated charcoal	
	B3: mitochondrial disease causing abnormal metabolism	Rare

3.14 Types and causes of hyperlactataemia together with an estimation of their prevalence in emergency and critically ill patients.
(Based on the classification by Cohen and Woods, 1976)

Central venous oxygen saturation

Central venous oxygen saturation ($S_{cv}O_2$) can be viewed as a reflection of the difference between oxygen delivery to and consumption by the tissues. When DO_2 decreases (due to anaemia, hypoxaemia or hypoperfusion) and/or VO_2 increases beyond a critical point, a decrease in $S_{cv}O_2$ results. $S_{cv}O_2$ in normal patients is about 65–75% (venous partial pressure of oxygen (P_vO_2) is approximately 40 mmHg); lower values indicate tissue dysoxia and oxygen debt. Although $S_{cv}O_2$ is not commonly directly measured in clinical practice, P_vO_2 is often substituted and under certain circumstances can be used clinically as an estimate of $S_{cv}O_2$). As long as the limitations and practical considerations regarding evaluation of these parameters is understood (discussed below), value may be gained by evaluating them in the diagnosis and treatment of shock.

First, sampling from peripheral sites (e.g. the cephalic vein) is not, in fact, 'central'; it will reflect only regional (e.g. the foot) and not global circulation. Thus, $S_{cv}O_2$ can only be usefully assessed using blood obtained from a central venous catheter. In veterinary medicine it is very unusual for a central venous catheter to be placed during initial shock resuscitation, although one may already be in place in a hospitalized patient. Second, most blood gas analysers measure P_vO_2; $S_{cv}O_2$ is then calculated from P_vO_2 via the oxyhaemoglobin dissociation curve, taking into account the temperature and pH. Thus, abnormalities in pH and temperature will confound interpretation of the values.

Historically, mixed and central venous oximetry have received a large amount of attention in human sepsis and critical care but in response to recent human trials, its use is currently being downplayed. These trials did not demonstrate superiority of use of central venous catheters for monitoring of $S_{cv}O_2$ (or central venous pressures), thus the sepsis improvement bundles were revised and routine placement of central venous catheters is no longer recommended.

The shock index (SI) is calculated by dividing heart rate by systolic blood pressure (SI = HR/SBP). A value greater than 0.9–1.0 has been associated with shock in dogs (Peterson *et al.*, 2013; Porter *et al.*, 2013). The shock index

is non-invasive and easy to calculate. Whilst evidence for its use in veterinary medicine is limited to date, it may prove clinically useful in dogs in the early stages of shock where the degree of tachycardia and hypotension may be subtle. A shock index >1.0 should prompt further investigation.

Veno-arterial carbon dioxide partial pressure gradient.

The venous partial pressure of carbon dioxide (P_vCO_2) is usually around 4–6 mmHg greater than the arterial partial pressure of carbon dioxide (P_aCO_2) because carbon dioxide is produced by tissue metabolism and venous blood carries it back to the lungs for elimination. During shock, a decrease in pulmonary blood flow (i.e. cardiac output) causes the difference between venous and arterial carbon dioxide pressures to increase. A difference >6 mmHg may indicate poor tissue perfusion.

Future diagnostic tests: assessment of microcirculatory perfusion

Traditionally, assessment has focused on global circulation in shock states. However, there is increasing evidence that global indices such as cardiac output do not correlate well with perfusion at the microcirculatory level (i.e. in the capillary beds). Techniques developed in human medicine for direct evaluation of microcirculatory changes have been evaluated in anaesthetized dogs (Silverstein *et al*., 2009) and dogs in haemorrhagic shock (Peruski *et al*., 2011). These techniques remain experimental at present, but this is an interesting area of active research and may provide valuable diagnostic tools for small animal veterinary medicine in the future.

Treatment

Rapid recognition and treatment of shock is vital to prevent irreversible cellular and tissue injury and reduce mortality. Initial treatment for some types of circulatory shock (hypovolaemic, obstructive, distributive) is rapid administration of intravenous fluids to improve tissue perfusion by restoring effective intravascular volume; therefore, the immediate priority is to gain vascular access. Vascular access techniques, advantages and disadvantages of sites and catheter types, and indications for each are described in Chapter 2. Acute resuscitative fluid therapy is discussed in Chapter 4. Thus, this section will focus on therapies that should be carried out in parallel with acute resuscitation, treatment of types of shock other than hypovolaemic, and special considerations when administering shock fluid therapy.

Adjunctive treatments in patients with shock

Adjunctive treatments during initial stabilization may include oxygen supplementation, analgesia, broad-spectrum intravenous antibiotics if sepsis is suspected, and corticosteroids if critical illness-related corticosteroid insufficiency (CIRCI) is suspected. Supplemental oxygen may be administered via flow-by or using a mask, nasal cannula/prongs or an oxygen cage/incubator (see Chapter 7). Although oxygen supplementation is unlikely to increase DO_2 dramatically without other resuscitative measures, it is quick and easy to implement and may help.

Prompt consideration should also be given to analgesia, particularly in patients that have sustained trauma, are presenting with an acute abdomen, or show signs of pain from other causes. Pain may exacerbate tachycardia, can increase myocardial oxygen demand, and can affect the vasomotor centre and interfere with the vasoconstrictive response. Typically, pure mu opioid agonist analgesics are appropriate in patients with shock, although at very high doses they may cause respiratory and cardiovascular depression. Non-steroidal anti-inflammatory drugs (NSAIDs) are contraindicated in shock patients because they may cause renal and gastrointestinal injury in the presence of hypoperfusion. Other analgesic options may include lidocaine and ketamine, which are often given as constant rate infusions (see Chapter 21).

If sepsis is present (based on known or suspected infection with consistent clinical signs), intravenous, broad-spectrum antibiotics should be started within 1 hour of the diagnosis of septic shock (see Chapter 23). This recommendation is an extrapolation from the Surviving Sepsis Guidelines for humans (Rhodes *et al*., 2017) and is reasonable to apply to veterinary patients (Butler, 2011) based on our knowledge of the pathophysiology of sepsis, and evidence from clinical and experimental animal models (see Treatment of distributive shock below).

Treatment of distributive shock

General considerations

Patients with distributive shock suffer from inappropriate vasodilatation and therefore require aggressive fluid resuscitation; in addition, they often need vasopressor support. At the same time, they typically have increased capillary permeability and hypoalbuminaemia and are therefore at risk of interstitial overhydration with fluid therapy, even in the face of intravascular volume depletion. These patients can be especially challenging to treat. Generally, acute resuscitative fluid therapy is commenced (see Chapter 4), and if the patient remains hypotensive (systolic arterial pressure (SAP) <80 mmHg; mean arterial pressure (MAP) <60 mmHg) despite reasonable attempts at fluid resuscitation, vasopressor treatment should be considered. Determining the point at which a persistently hypotensive patient will not benefit from further intravenous fluid boluses can be difficult. Measuring central venous pressure (CVP) can aid in predicting volume responsiveness; however, several factors can confound the interpretation of this therapeutic endpoint. Although its utility is debated, in the absence of other alternatives, CVP monitoring remains one of the few options available to general practitioners (Marik and Cavallazzi, 2013) (see Chapters 2 and 4, as well as Monitoring shock resuscitation below).

The 2016 Surviving Sepsis Guidelines recommend that resuscitation by performed by administering 30 ml/kg isotonic crystalloid fluid aliquots (saline or a balanced isotonic but not synthetic colloid solution) for as long as haemodynamic parameters improve, and monitoring using dynamic response testing (i.e. passive leg raises) and frequent reassessment, with the goals of normalizing lactate and attaining a mean arterial blood pressure of >65 mmHg. It has been suggested to aim for a 50% reduction in lactate concentrations in the first 1–2 hours of resuscitation (Rosenstein *et al*., 2014).

Patients with suspected CIRCI (i.e. patients that are hypotensive despite volume resuscitation and are vasopressor-dependent) may benefit from replacement treatment with hydrocortisone after adrenocorticotropic

hormone (ACTH) stimulation testing. If ACTH stimulation evokes a normal cortisol response, therapy may be discontinued. Therapy may be continued if: the basal cortisol level is normal but the ACTH-stimulated cortisol concentration is still below the reference range; there is a normal or elevated basal cortisol concentration but a 'flatline' (<5%) response; the response is <3 μg/dl (830 nmol/l) above the basal cortisol concentration; or there is a clinically significant positive cardiovascular response upon corticosteroid replacement therapy. General non-specific use of steroids for shock, especially at higher doses, has not been shown to be beneficial and is discouraged since it may be associated with adverse gastrointestinal effects.

Vasopressor and inotropic therapy

Studies are ongoing to determine whether any one vasopressor is better than another in veterinary patients. At present, it is reasonable to start with either noradrenaline (norepinephrine) or dopamine; vasopressin may also be considered. Noradrenaline is recommended as the first-choice vasopressor in humans with septic shock (Rhodes *et al*., 2013). Noradrenaline is a catecholamine that mainly acts at alpha receptors, which are found on vascular smooth muscle cells; stimulation of alpha receptors results in vasoconstriction. Dopamine also stimulates alpha receptors at the higher end of the dose range, and as such may be useful in vasodilated patients. It also stimulates dopaminergic and beta receptors at the lower and middle dose ranges, respectively.

Vasopressin is not a catecholamine but acts via vasopressin receptors on vascular smooth muscle to cause vasoconstriction; it may be useful in patients that are not responsive to catecholamines. There is increasing interest in both human and veterinary medicine in the use of vasopressin to treat vasodilatory shock. However, at present it is expensive and difficult to source in the UK.

Dobutamine has its greatest effect at beta-1 receptors and as such is generally considered an inotropic (not a vasopressor) agent. Dobutamine may be useful when reduced cardiac contractility (e.g. sepsis-induced myocardial dysfunction) is suspected. It should be noted that this drug also has mild beta-2 effects and as such can cause mild vasodilation. Of note, dobutamine has been reported to cause central nervous system effects (tremors and seizures) at higher doses in cats.

Vasopressors are administered as constant rate infusions; the dose ranges and mechanisms of action are summarized in Figure 3.15. If vasopressors are started, ongoing monitoring of fluid status and haemodynamics is essential (see Chapter 4). Direct (invasive) blood pressure monitoring is ideal when patients are treated with vasoactive medications because it provides continuous real-time information about the response to therapy, and has the greatest likelihood of accuracy in the presence of hypotension. If using non-invasive (indirect) means of measurement (e.g. Doppler or oscillometric), arterial blood pressure should be monitored at least every 15–30 minutes initially and after dose changes, and at least every 4 hours once the patient is stable. Vasopressors can cause cardiac arrhythmias, tachycardia and hypertension, so continuous electrocardiogram (ECG) monitoring is essential. Although vasopressors can increase arterial blood pressure, they may result in splanchnic vasoconstriction, which can cause gut and renal ischaemia, thereby potentiating organ dysfunction and failure. Thus, initiating the process of discontinuing vasopressor therapy should be considered when the underlying disease has been addressed and/or the patient's clinical status is improving. At this stage, vasopressor therapy should be gradually tapered, with close cardiovascular monitoring, over 6–18 hours.

Agent	Mechanism of action	Dose range
Vasopressor agents		
Noradrenaline	Catecholamine causing mainly alpha adrenergic stimulation and peripheral vasoconstriction	0.05–2 μg/kg/min
Dopamine	Catecholamine with mixed alpha and beta adrenergic stimulation causing peripheral vasoconstriction, increased cardiac contractility and heart rate	5–15 μg/kg/min
Vasopressin	Stimulation of vasopressin receptors on vascular smooth muscle causing peripheral vasoconstriction	0.5–2 mU/kg/min
Inotropic agents		
Dobutamine	Catecholamine causing mainly beta-1 adrenergic stimulation, resulting in increased cardiac contractility, and mild beta-2 effects (vasodilation)	2–20 μg/kg/min (dogs)

3.15 Dose ranges and mechanisms of action of vasopressor and inotropic agents.

Source control and antimicrobial therapy

In distributive shock patients, the septic or inflammatory focus should be removed as quickly as possible and the patient should be treated with antimicrobial drugs as soon as sepsis is known or suspected. Ideally, appropriate samples should be collected for culture and sensitivity testing prior to starting broad-spectrum intravenous antibiotic treatment, but if samples cannot be collected quickly, antibiotic treatment should not be delayed in these critical patients. There is good evidence in human medicine that delivery of appropriate antibiotics very early in the treatment of septic shock has a significant positive effect on outcome; the current recommendation is to commence antibiotic therapy within 1 hour of the recognition or suspicion of sepsis and septic shock (Rhodes *et al*., 2017).

Antibiotics should be reassessed once culture results are back and adjusted as appropriate (changed if necessary or the spectrum narrowed). A rational choice of antibiotics is essential to improve survival, and suggestions for appropriate combinations of intravenous antibiotics to provide broad-spectrum coverage can be found in Chapter 23.

Intervention to remove the source of infection whenever possible ('source control') is vital, and should ideally be performed as soon as it is medically and logistically possible. However, surgical intervention may carry a high risk in an unstable patient; therefore resuscitation should take priority, and the simplest surgical plan to treat the infection with the least risk to the patient should be instituted until the patient is more stable. Anaesthesia and surgery should be thought of as subsequent 'hits' (in addition to the infection and shock) that may contribute to the overall morbidity of the patient. Despite this, it is essential that source control be performed as soon as possible after the patient is stabilized. Occasionally, despite aggressive attempts at stabilization, it can become clear that no further improvement in haemodynamics will occur without source control. It can be a difficult decision to move forward with source control; however, the benefits may outweigh the risks in these patients.

Treatment of obstructive shock

Treatment for obstructive shock depends on the underlying cause. Patients with obstructive shock are often hypovolaemic, and as such require fluid therapy in addition to treatment of the underlying cause of obstructed blood flow. Typical causes of obstructive shock include pericardial tamponade, GDV, restrictive pericarditis and pulmonary thromboembolism. Treatment is aimed at the underlying cause (e.g. pericardiocentesis or gastric decompression; see Chapters 6 and 12). Particular consideration of the catheter site for intravenous fluid therapy is warranted in patients with GDV; this form of obstructive shock causes impairment of venous return through the caudal vena cava, so a thoracic limb or central vein (e.g. cephalic or jugular vein) should be used for administration of shock fluid therapy in these patients.

Treatment of cardiogenic shock

Treatment for cardiogenic shock differs from treatment of other forms of circulatory shock as fluid resuscitation should be used with caution, if at all, in patients with increased risk of fluid overload. Instead of fluids, the mainstay of treatment is addressing the underlying disease with appropriate medication or procedures (see Chapter 6). These can often be very unstable patients and care should be taken to minimize stress. Full physical examination and diagnostics (such as thoracic radiography) are often delayed until the patient is stable enough to cope with restraint. In the interim, oxygen supplementation should be provided, and if signs of congestive heart failure are present then furosemide should be administered intravenously (if a catheter has been placed) or intramuscularly at an initial dose of 2 mg/kg (cats) or 4 mg/kg (dogs), with follow-up doses as needed based on the clinical response. Additional therapy in dogs could include a positive inotrope if there is decreased cardiac contractility, or antiarrhythmics as indicated (see Chapter 6).

Special considerations and troubleshooting ineffective fluid therapy

The decision to treat with aggressive intravenous fluid therapy should prompt careful consideration of any reason to be particularly cautious with the fluid volumes administered, e.g. hypovolaemic patients with concurrent lung injury or patients with pre-existing heart murmurs. Caution is also warranted in cats, which seem to be more susceptible than dogs to pulmonary oedema and pleural effusion with aggressive resuscitative fluid therapy. This may be partly because the lungs are the 'shock organ' of the cat and seem to be susceptible to both permeability and hydrostatic oedema in the setting of shock and critical illness, and also because the blood volume of the cat is smaller than that of the dog.

For any patient in which there is concern about fluid administration, more advanced monitoring may be warranted (e.g. CVP monitoring), and referral to a secondary or tertiary care facility may be advisable. If acute resuscitative fluid therapy is ineffective, or less effective than expected, complicating factors should be taken into consideration (e.g. ongoing haemorrhage, systolic dysfunction, vasodilatation or endocrine problems such as CIRCI; see above).

Hypotensive resuscitation

Experimental animal models have shown increased mortality when early, aggressive fluid resuscitation is used in cases of uncontrolled haemorrhage. Fluid resuscitation may cause changes in blood viscosity, dilution of clotting factors, or mechanical disruption of clots, all of which could exacerbate haemorrhage. Limited clinical studies in humans suggest that hypotensive resuscitation (i.e. deliberately targeting a lower MAP (e.g. 60 mmHg) until haemorrhage has been fully controlled ('damage control')) may be beneficial in severe trauma, but the concept remains controversial. In any case, this approach should only be taken if definitive steps towards controlling the source of haemorrhage are being taken simultaneously with the hypotensive resuscitation. Due to the fact that, for practical reasons, veterinary patients may not receive definitive management of haemorrhage immediately (as is the case with humans), this approach has to be viewed sceptically. No veterinary studies have been performed. Hypotensive resuscitation is contraindicated in cases of traumatic brain injury (discussed below).

Pulmonary contusions

Animals that have sustained blunt trauma are frequently presented with pulmonary contusions in combination with other injuries that result in shock. In these cases, increased vascular permeability within the pulmonary parenchyma predisposes the patient to worsening pulmonary oedema when intravenous fluids are administered. This exacerbation of pulmonary oedema by volume resuscitation means that cautious use of fluids is important. Crystalloid fluids will be redistributed into the pulmonary interstitium, and the resulting increased lung water further compromises oxygen exchange. The use of hypertonic saline and colloids has therefore been recommended by some authors to provide comparative resuscitation with lower volumes of fluid. However, these types of fluid do not necessarily prevent accumulation of fluid in the interstitium of the lung, and there is no evidence that this is a superior resuscitation strategy.

Clinical management of these patients can be difficult. Resuscitation with small aliquots of fluid is recommended, with close observation to ensure that fluid rates are tapered as soon as resuscitation endpoints are met. Transfusion of blood products may be better tolerated than other types of fluid. Oxygen supplementation and ongoing monitoring of oxygenation during resuscitation are essential. Use of catecholamines such as dopamine may be considered for cardiovascular support earlier during resuscitation, if fluid administration must be limited or curtailed. Mechanical ventilation is indicated if haemodynamic stability cannot be achieved without compromising lung function.

Traumatic brain injury

There is good evidence from human medicine that even short periods of hypotension can greatly increase mortality from traumatic brain injury. Hypotension causes decreased cerebral perfusion pressure, which potentiates secondary brain injury. Historically, fluid therapy was withheld from patients presenting with head injury and concurrent shock in the belief that it would worsen cerebral oedema. However, in light of new evidence, current recommendations are for aggressive fluid resuscitation in this patient population.

Much debate remains as to the ideal choice of fluid for initial resuscitation. There is increasing interest in human medicine in the beneficial effects of hypertonic saline for traumatic brain injury. Hypertonic saline has been shown

to reduce intracranial pressure and to decrease neuronal excitotoxicity. Although to date there is insufficient evidence to recommend its use as a sole agent to reduce intracranial pressure, this remains an area of active research. Hypertonic saline also provides rapid intravascular volume resuscitation at low fluid volumes. Its combined volume-expanding and neuroprotective properties theoretically make it a good first choice fluid for resuscitation in patients with traumatic brain injury. It should be kept in mind that hypertonic saline is a crystalloid solution that will redistribute rapidly, thus ongoing intravascular monitoring and support must be provided, and concurrent use of isotonic crystalloids or colloids may be considered in an effort to maintain the otherwise transient gains in intravascular volume.

Monitoring shock resuscitation

Each patient in shock responds to treatment differently, and given the life-threatening nature of this condition it is essential to assess the response and to determine whether adequate treatment has been provided. There is much controversy in human and veterinary medicine over the 'endpoints of resuscitation' that should be targeted for optimal outcome, and this is an area of active research. Even after normalization of vital signs and global haemodynamic parameters, such as arterial blood pressure and heart rate, patients may have ongoing tissue hypoxia and remain in a compensated state of shock or 'cryptic shock.' In other words, macrohaemodynamic stabilization does not always mean that tissue dysoxia has been resolved because microhaemodynamics are often persistently abnormal even after global haemodynamic variables have normalized.

Basic monitoring

Physical examination

The major body system assessment should be repeated at regular intervals during resuscitation, and frequently thereafter (see above and Chapter 1). Typically, patient examination is repeated at least every 15–30 minutes during initial stabilization, then at least every 4 hours. Normal mentation, respiratory rate and effort, heart rate, pulse quality, temperature of the extremities and rectal temperature should be targeted.

Arterial blood pressure

Decreased cardiac output in circulatory shock often, but not always, results in hypotension. Arterial blood pressure is the product of cardiac output and systemic vascular resistance. It is important to note that arterial blood pressure within the normal range does not necessarily equate to adequate tissue blood flow and tissue perfusion. If systemic vascular resistance is increased due to compensation, pain or for other reasons, arterial blood pressure may be normal or high (less commonly) in the face of mildly to moderately reduced cardiac output. Arterial blood pressure measurement, although useful both in initial assessment and for monitoring resuscitation, should therefore be interpreted with caution in patients with shock and should always be considered in combination with heart rate and basic physical examination parameters of systemic perfusion (such as temperature of the extremities). In hypotensive patients, normalization of blood pressure within the first hour of fluid resuscitation has been correlated with improved outcomes in veterinary patients (Silverstein *et al*., 2012).

Arterial blood pressure can be measured directly or indirectly. Direct measurement is the gold standard and involves placement of an intra-arterial catheter connected via a pressure transducer to a monitor that displays the arterial waveform and gives continuous pressure readings. Placement of arterial catheters requires some technical expertise (see Chapter 2), and direct pressure monitoring requires equipment that is not routinely available.

Indirect (non-invasive) blood pressure monitoring is therefore more commonly used in veterinary medicine. Doppler and oscillometric methods are available. In both methods a cuff is applied around an extremity, usually the distal limb over the radial or dorsal pedal artery. A cuff width of approximately 40% of the circumference of the extremity is used. If the cuff is too wide, readings will be falsely low, and if it is too narrow, readings will be falsely high. If using the Doppler method, the area is clipped and coupling gel is applied with the flow detector crystal placed over the artery. The cuff is then inflated until it occludes arterial blood flow. The air in the cuff is slowly released while the reading on the sphygmomanometer is observed gradually decreasing; the reading at which the signal is first audible is widely accepted to represent SAP. Doppler blood pressure measurement is useful in patients of any size, but particularly cats and small dogs, and in patients with arrhythmias. Limitations of this method are that mean and diastolic arterial pressures are difficult to measure reliably.

With the oscillometric method, the cuff is inflated and deflated by a machine that detects oscillatory pressure changes in the cuff caused during pulsation of the underlying artery as the cuff is deflated. Systolic, diastolic and mean pressures are reported, with MAP believed to be most accurate. Several oscillometric machines have been evaluated for use in veterinary medicine, and it is important to make sure that the system in use has been appropriately validated. For example, some machines are not reliable for use with cats. It may be difficult to obtain readings with oscillometric machines in patients that are tachycardic or have arrhythmias. Some machines have a continuous cycling feature, which enables automated blood pressure measurements at a frequency that is determined by the user. This can be useful during resuscitation and in unstable patients. Normal blood pressure values in dogs and cats are summarized in Figure 3.16. The MAP may be calculated using the formula:

$$MAP = DAP + \tfrac{1}{3}(SAP - DAP)$$

Where:

DAP = diastolic arterial pressure
MAP = mean arterial pressure
SAP = systolic arterial pressure.

Hypotension is defined as a SAP <80 mmHg or a MAP <60 mmHg.

Species	Systolic pressure (mmHg)	Diastolic pressure (mmHg)
Dogs	110–190	55–110
Cats	120–170	70–120

3.16 Normal arterial blood pressure values in dogs and cats.

Central venous pressure

CVP is the blood pressure in the cranial vena cava near the right atrium. It is used to approximate the pressure within the right atrium as an estimate of preload (left ventricular end-diastolic volume). Placement of a central venous catheter may not be appropriate or practical for all patients in shock, but monitoring CVP may be useful both during initial resuscitation and in the post-resuscitative period, particularly in patients at risk of fluid overload (e.g. with cardiac disease or oligoanuric renal failure).

Placement of a central venous catheter is described in Chapter 2, and interpretation of changes in response to fluid resuscitation is described in Chapter 4. Briefly, volume responsiveness can be inferred if rapid administration of a 20 ml/kg crystalloid (or 5 ml/kg colloid) fluid bolus to a hypovolaemic patient causes the CVP to increase minimally (e.g. by 0–2 mmHg) with a subsequent rapid return to the baseline (within 10 minutes). In addition, other monitoring parameters should indicate improved perfusion, suggesting volume responsiveness. The 'test' bolus should be administered very quickly to prevent the venous system accommodating the volume and hence blunting the CVP response. If the bolus causes the CVP to increase by more than 2 mmHg and it stays elevated without any further evidence to indicate improved perfusion, this suggests that the patient is not volume responsive. If the CVP increases by more than 4 mmHg, or if it takes more than 30 minutes to return to normal, this could suggest decreased cardiac function or increased vascular volume, in which case additional fluids may be detrimental.

Lactate clearance

In humans, serial lactate measurements with analysis of the percentage decrease in lactate over time has been found useful in predicting outcome. Recent studies in veterinary medicine show similar results (Stevenson *et al*., 2007; Green *et al*., 2011). To date, these reports are small and retrospective, but future studies may provide useful information to guide treatment and prognosis. Current expert opinion in combination with the strong evidence that lactate clearance is highly important suggests to aim to reduce lactate concentration by 50% within 1–2 hours (Rosenstein, 2014).

Urine output

In patients with shock, hypoperfusion of the kidneys reduces the glomerular filtration rate, resulting in decreased urine output. Measurement of urine output can therefore be useful to guide fluid resuscitation in these patients. This is most accurately performed by placing an indwelling urinary catheter with a closed collection system and measuring output every 2–4 hours. Urine production >0.5 ml/kg/h is targeted (see above). Interpretation of urine output may be complicated by the presence of acute kidney injury (resulting in polyuria or oliguria) or by comorbidities causing polyuria, such as diabetes mellitus. Where confounding factors are suspected further diagnostic tests are warranted such as measurement of urine specific gravity, urinalysis and sediment examination.

ECG monitoring

Continuous ECG monitoring is a useful tool in any patient with shock, regardless of the underlying cause. Cardiac dysrhythmias should initially be ruled out as a cause of shock, but may develop as a sequela of shock both during and in the hours following resuscitation.

Prognosis for shock

The prognosis for shock depends upon the underlying cause and the stage of the clinical syndrome. Many of these patients sustain multiple 'hits' that contribute to a difficult recovery and poorer prognosis (e.g. the initial insult, shock, ischaemia-reperfusion injury, infection, anaesthesia, surgery). Overall, these patients can be extremely rewarding to treat; however, intensive care and monitoring is required. Admission to the hospital is always recommended; if intensive and 24-hour care cannot be offered, referral should be considered.

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Chapter 4

Fluid therapy

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Fluid therapy is part of the treatment plan in most critically ill animals. In some patients fluid therapy is used acutely to treat absolute or relative intravascular volume deficits over a period of minutes to hours. Alternatively, fluid therapy may be used on a more chronic basis, during treatment of the haemodynamically stable patient, to re-establish and maintain normal water, electrolyte and acid–base balance over a period of several days. The precise type, rate and total volume of fluid to be administered for optimal management of a patient can be difficult to determine, especially at the beginning of treatment, and fluid therapy plans may need to be altered depending on the patient's response and the progression of the disease.

Unfortunately, there are no 'recipes' that can be followed that will guarantee a successful outcome. Good fluid management comes from understanding why the patient requires fluid therapy, and considering both the goals of fluid administration in that patient and the advantages and disadvantages of the different fluid types in achieving those goals. Goal-directed fluid therapy, where the volume of fluids administered is decided upon on the basis of achieving specific measurable endpoints, is now widely considered to be best practice (Rhodes *et al*., 2017). In assessing the fluid therapy requirements of an animal, it is extremely important to separate those patients requiring life-saving intravascular volume expansion from those requiring a more gradual correction, or maintenance, of fluid and electrolyte balance. Central to this goal is an appreciation of the difference between hypoperfusion and dehydration.

Hypoperfusion refers to a local or generalized deficit in tissue blood flow, which results in inadequate oxygen and nutrient delivery and failure to remove metabolic by-products from the tissues. Global hypoperfusion can occur due to hypovolaemia (a reduction in the effective circulating intravascular volume), reduced cardiac function, maldistribution of blood flow such as that seen in the systemic inflammatory response syndrome (SIRS), or physical obstruction to blood flow if it occurs close to the heart (see Chapter 3). Hypovolaemia is the most common cause of hypoperfusion. Common causes of hypovolaemia include: haemorrhage; extracellular fluid losses in excess of fluid and solute intake, such as vomiting, diarrhoea and polyuria; and internal losses of plasma volume due to exudation or transudation of fluid from the intravascular space ('third-spacing'). Most animals with SIRS and some animals with cardiogenic shock also have concurrent reductions in effective circulating intravascular volume.

Dehydration is strictly defined as a net reduction in the free water content of the body; however, in veterinary patients the term is most often used to refer to combined water and solute loss in excess of intake. Dehydration may ultimately lead to hypovolaemia and hypoperfusion depending upon the volume and nature of the fluid that is lost; however, the terms are not synonymous.

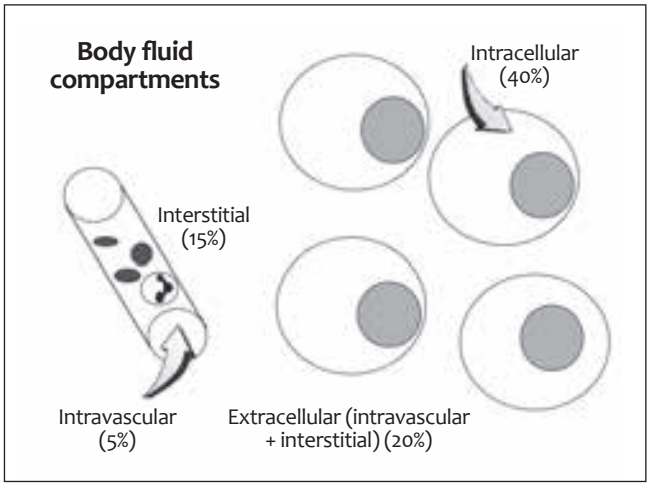
Understanding whether fluid therapy is being used to treat a perfusion abnormality, a hydration abnormality, a combination of the two, or to prevent development of one or both of these is crucial to providing good fluid therapy. Both perfusion and hydration abnormalities are initially evaluated using the physical examination. Unfortunately, the parameters used for assessment of hydration status (moisture of the mucous membranes, skin turgor, presence or absence of retraction of the globe) are often combined with those used to assess perfusion (heart rate, pulse quality, mucous membrane colour and capillary refill time). This combination of hydration and perfusion parameters has compounded the confusion between the terms and should be avoided.

To illustrate the difference, consider a dog hit by a car 1 hour previously, which has suffered a fractured spleen and bled half of its blood volume into its peritoneal cavity. This animal would have no net change in the water content of its body and no physical examination findings suggestive of dehydration; however, it would be severely hypovolaemic. In contrast, the geriatric cat with anorexia, hypodipsia and chronic renal failure, with prolonged net water loss in excess of intake, may be severely dehydrated but often has surprisingly good perfusion status. The former animal would require rapid intravascular volume replacement to re-expand effective blood volume and thereby preserve perfusion to the major body systems. In the latter animal, in which perfusion of major organs is adequate, more conservative fluid therapy would be appropriate with a goal of re-establishing normal fluid and electrolyte balance over 24–48 hours. A clear understanding of the distinction between dehydration and hypovolaemia and the clinical assessment of both conditions is therefore necessary to ensure appropriate fluid therapy.

Extracellular fluid homeostasis – physiology review

To understand the choice of intravenous fluids, it is necessary to appreciate how fluids are normally distributed within the body and the factors that control movement of fluid between different compartments. Three major fluid

compartments make up the total body water: the intracellular fluid; the interstitial fluid between cells; and the intravascular fluid (Figure 4.1). Together the intravascular and interstitial fluids comprise the extracellular fluid compartment. Total body water is approximately 60% of total bodyweight; however, this may vary depending upon such factors as the species, the age of the animal and the body composition (mainly the fat content). Movement of fluid between compartments depends upon the permeability of the relevant barrier and the concentration of molecules contained within each compartment. Importantly, the capillary endothelium is freely permeable to water and electrolytes, whereas the cell membrane is freely permeable only to water. Movement of water across the cell membrane depends upon the relative concentration of solute molecules within cells compared with the concentration around the cell. Net movement of water will occur by osmosis into an area with a higher concentration of solute molecules; this has important implications in disease (see Figures 4.2 and 4.3).



4.1 Major fluid compartments of the body (% of bodyweight).

Control of extracellular volume and concentration

Extracellular fluid homeostasis in the normal animal is controlled by two distinct, but intertwined, feedback loops. One system acts to maintain the concentration, or osmolality, of the body and one regulates the volume of the extracellular fluid. It is important to remember that no distinction is made between intravascular fluid and interstitial fluid because the capillary membrane is extremely permeable to water and small solutes.

Osmolality is controlled by hypothalamic osmoreceptors that stimulate thirst and the release of antidiuretic hormone (ADH) from the neurohypophysis. If net water loss from the body exceeds net water gain, plasma osmolality will rise and hypothalamic osmoreceptors then stimulate thirst and release of ADH. The augmented water intake and increased reabsorption of water by the kidney combine to decrease plasma osmolality towards normal. Fluctuations in plasma osmolality necessary to stimulate thirst and ADH release are very small (approximately 4 mOsm/kg in the dog, i.e. an increase in plasma sodium concentration of only 2 mmol/l).

Extracellular volume is primarily dependent upon total body sodium content, controlled by the renin–angiotensin–aldosterone system and modulated by the natriuretic peptides. Sympathetic discharge and decrease in stretch of renal afferent arterioles stimulate renin release from the juxtaglomerular cells. Renin activates angiotensinogen to angiotensin I, which is then converted to angiotensin II. Sodium and water reabsorption is increased by angiotensin II in the proximal tubule and angiotensin II-mediated aldosterone release promotes distal tubular sodium reabsorption.

The feedback loops controlling extracellular volume and osmolality overlap as they can both cause ADH release and thirst. During hypovolaemia, the renin–angiotensin–aldosterone system, ADH and thirst act to increase retention of sodium and water and to expand extracellular volume. In summary, the *concentration* of the extracellular fluid is controlled primarily via modulation of water balance, whereas the *volume* of the extracellular fluid is regulated by changes in sodium and water balance.

Maintenance of intravascular volume

Adequate intravascular volume is essential for maintaining perfusion. As capillaries are relatively (but not completely) impermeable to macromolecules, a protein concentration gradient exists from the vasculature to the interstitium. The higher concentration of impermeant solutes within the capillaries exerts an osmotic pressure (termed the capillary colloid osmotic pressure (COP)) which acts to retain fluid in the vasculature. Fluid flux out of the vessel is predominantly due to hydrostatic forces with lymphatic drainage being responsible for removal of fluid from the interstitium. The role of intravascular and interstitial COP in transvascular fluid flows are much less important than previously thought. Although the microvascular barrier greatly restricts macromolecular flux, capillaries are slightly permeable to protein. Of the total quantity of albumin present in the body, 40% is intravascular and 60% is extravascular. Furthermore, all the albumin present in plasma circulates through the interstitium every 24 hours. It is important to note that the permeability of the microvascular barrier varies between tissues. For example, the microvascular barrier of skeletal muscle or subcutaneous tissue is relatively impermeable to protein, whereas the pulmonary capillary endothelium is more permeable. Different plasma proteins or artificial colloid molecules will differ in their rate of efflux from a vessel depending upon such factors as their molecular radius, shape and charge. Smaller plasma proteins, such as albumin, can pass through with less impedance than larger plasma proteins. In healthy animals, the hydrostatic and osmotic pressure gradients governing transvascular fluid flux and the permeability of the microvascular barrier can vary between different tissues and at different levels of the capillary bed within the same tissue; these may vary even further with different disease states.

By virtue of its relatively high concentration in the vascular space, albumin usually accounts for 80% of the plasma COP, with globulins making up the remainder. Albumin synthesis, which is unique to the liver, is regulated by the hepatic plasma COP. Equations have been calculated to estimate plasma COP from plasma protein concentrations; however, direct measurement, using a colloid osmometer, is more accurate. Normal COP in dogs is approximately 16–24 mmHg.

Excess fluid in the interstitium (oedema) can have detrimental consequences, the exact nature of which depends on the anatomical site. Two major mechanisms guard against interstitial fluid accumulation. First, extravasation of fluid into a relatively non-distensible interstitium results in an increased interstitial pressure, which thereby opposes

further extravasation. Second, because the interstitium is not compliant, increased interstitial fluid results in an increased driving pressure for lymphatic drainage, which is the major mechanism by which interstitial fluid is drained. These alterations in Starling forces, which act to limit interstitial fluid accumulation, have been termed the 'tissue safety factors'. Their relative importance varies depending upon the characteristics of the tissue. In a relatively non-distensible tissue such as tendon, a rise in interstitial pressure may be the most important means by which to counteract filtration. In a tissue with moderate distensibility and a relatively impermeable microvascular barrier, such as skin, the fall in interstitial COP assumes more importance in protecting against interstitial fluid accumulation. In a distensible tissue that is quite permeable to protein, such as the lung, increased lymph flow appears to be the most important safeguard against interstitial oedema.

Because of this marked heterogeneity in Starling forces and transvascular fluid dynamics between tissues, it is a potentially dangerous oversimplification to view the body as the homogenous sum of its individual parts. A great deal of emphasis has been placed on the manipulation of individual Starling forces in isolation, such as the intravascular COP with the use of colloid fluids, rather than addressing the system in its entirety. The effects of this manipulation on different tissues and organ systems should be carefully considered, especially if microvascular permeability is likely to be altered. The role of the endothelial glycocalyx (the layer of membrane-bound proteoglycans and glycoproteins on the luminal side of the endothelial cells) is an area of active research, and a better understanding of how it behaves in health and in disease will further improve our ability to tailor fluid therapy to specific patients and has radically changed our understanding of transvascular fluid flux (Woodcock and Woodcock, 2012; Ushiyama *et al*., 2016). If a COP gradient cannot be maintained between the intravascular and interstitial spaces then the capillary hydrostatic pressure becomes the major determinant of fluid extravasation. Smaller rises in capillary hydrostatic pressure will result in much greater fluid extravasation than when the endothelium remains intact. From a clinical standpoint, the differences between transvascular fluid flux in the lungs compared with the systemic circulation are the most important.

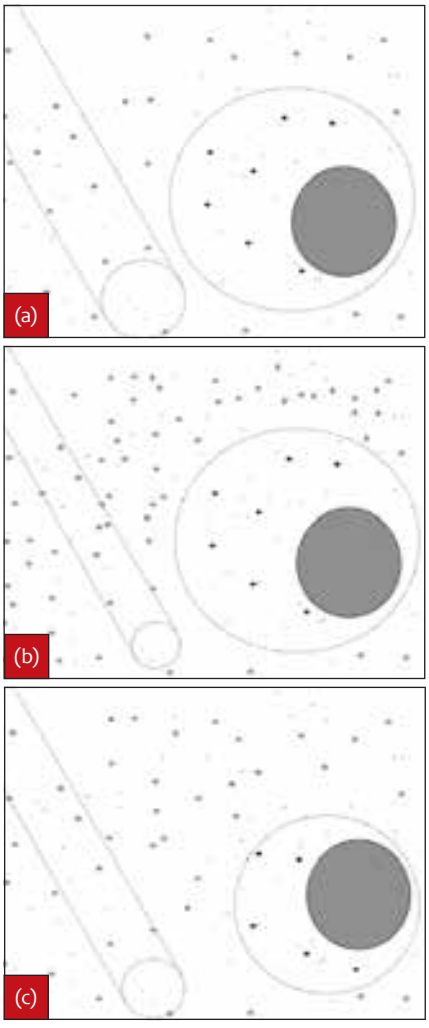
Maintenance of arterial blood pressure

With acute or severe reductions in effective circulating blood volume, the body reacts to maintain arterial blood pressure and effective circulating blood volume to the heart, lungs and brain. With mild to moderate degrees of hypovolaemia, baroreceptor reflexes initiate sympathetic discharge, causing an increase in heart rate and cardiac contractility and, to a lesser degree, vasoconstriction. This is the so-called 'compensatory' or 'hyperdynamic' phase of hypovolaemia, when mean arterial blood pressure is maintained. After moderate reductions in blood volume, cardiac compensatory mechanisms are insufficient but vasoconstriction in the peripheral and splanchnic circulation increases to maintain arterial blood pressure; although there is partial compensation with maintenance of blood flow to vital organs, this stage of moderate hypovolaemia is associated with poor perfusion to some organs, notably the gastrointestinal (GI) tract. Ultimately, after severe reductions in blood volume, despite a maximum response from counter-regulatory mechanisms, progressively falling blood volume results in a fall in arterial blood pressure, the so-called 'decompensatory' or 'hypodynamic' phase of hypovolaemia.

Pathophysiology of abnormal fluid losses

In a normal animal, fluid is lost in urine and faeces and via evaporation from the respiratory tract. Abnormal losses include vomiting and diarrhoea, polyuria, increased body temperature and panting, bleeding, wound exudation, loss from chest or abdominal drainage tubes, and loss into the interstitium or body cavities (often called 'third-spacing'). The effect of fluid loss on intravascular volume depends upon the magnitude of the loss, and on the water shifts that occur between the extra- and intracellular spaces as a result of changes in extracellular fluid concentration. These water shifts depend upon the tonicity (concentration) of the extracellular fluid lost relative to the intracellular fluid.

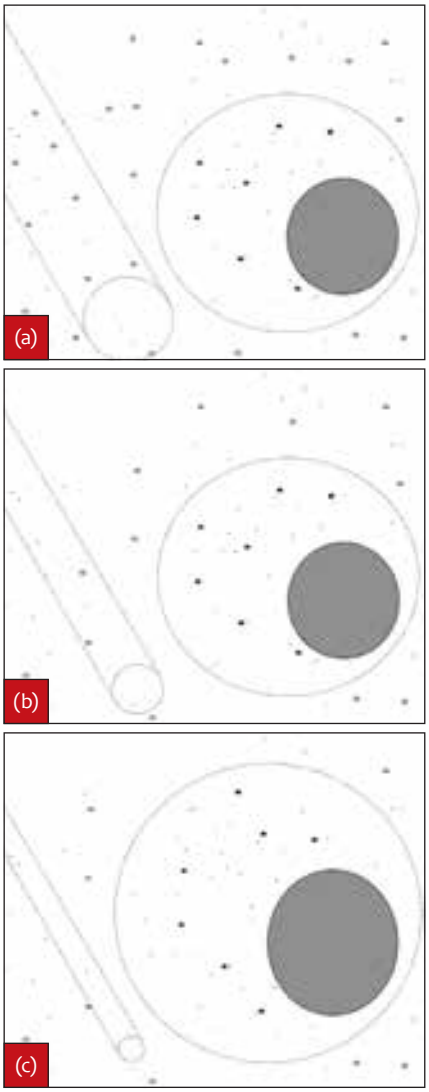
Loss of pure water or hypotonic fluid causes the extracellular fluid to become more concentrated compared with the intracellular space. Water moves out of cells, thereby supporting extracellular (and therefore intravascular) volume (Figure 4.2). This type of fluid loss is uncommon but occurs, for example, in animals that produce large volumes of hyposthenuric urine because of diabetes insipidus. The fluid loss is distributed over the total body water and intravascular depletion is a small proportion of the total loss. With loss of isotonic fluid (for example, with bleeding or in animals with surface losses through burn or bite wounds) no water movements occur because there is no change in extracellular concentration to create an osmotic gradient.



4.2 (a) Normal fluid volumes and concentration. (b) Hypotonic fluid loss results in a reduced plasma volume and increased concentration of the extracellular fluid. An osmotic gradient exists, which favours the movement of water from the intracellular to the extracellular space. (c) Water moves out of the cells to buffer the reduction in extracellular fluid, thereby supporting the intravascular volume. The major extracellular cation is sodium (○) and the major intracellular cation is potassium (●). Small dots represent water molecules.

With hypertonic fluid loss, the extracellular space becomes hypotonic relative to the intracellular space and water moves into cells, exacerbating the extracellular fluid deficit and hypovolaemia (Figure 4.3). The very acute and severe haemoconcentration and hypovolaemia seen in haemorrhagic gastroenteritis in dogs is an example of hypertonic fluid loss, ostensibly due to a secretory diarrhoea.

To illustrate the effects of fluid loss on intravascular volume status, consider a dog with dehydration due to water restriction alone. Dehydration of 12% of bodyweight would imply a free water deficit of 120 ml/kg. As water moves freely across cell membranes, this loss would be shared equally between the intravascular, interstitial and intracellular fluid compartments. Assuming that the free water deficit is distributed between these compartments on the basis of their relative size (i.e. 1:3:8 or 5, 15 and 40% of bodyweight, respectively; see Figure 4.1), one twelfth of the fluid loss would be borne by the intravascular compartment. This would result in a decrease in intravascular volume of approximately 10 ml/kg, an amount comparable with the volume of blood normally removed from a canine blood donor, usually with few or no untoward effects. Conversely, with loss solely from the intravascular space, i.e. haemorrhage, loss of 5% of bodyweight (i.e. 50 ml/kg or more than 50% of the blood volume) would result in clinical signs of severe hypovolaemia.



4.3 (a) Normal fluid volumes and concentration. (b) Hypertonic fluid loss results in a reduced plasma volume and a reduced concentration of the extracellular fluid. An osmotic gradient exists, which favours the movement of water into cells from the extracellular space. (c) Water movement into the cells exacerbates the reduction in intravascular volume. The major extracellular cation is sodium (○) and the major intracellular cation is potassium (●). Small dots represent water molecules.

Approach to fluid therapy in the clinical patient

The approach to fluid therapy suggested by DiBartola and Bateman (2012) is helpful when deciding upon a fluid therapy plan.

- Does the animal require fluid therapy?
- What type or types of fluid should be given?
- Which route should be used?
- How much should be given?
- Over what time period should it be administered?
- For how long should therapy be continued?

Careful consideration of the first question with critical evaluation of whether the animal requires fluid therapy to treat hypoperfusion, to treat dehydration, or for maintenance purposes (or some combination of those three) will allow the subsequent questions to be answered and the fluid therapy plan to be tailored to that patient's needs. As hypoperfusion represents an imminently life-threatening situation for the patient, abnormalities of perfusion should always be corrected prior to considering the longer-term fluid requirements.

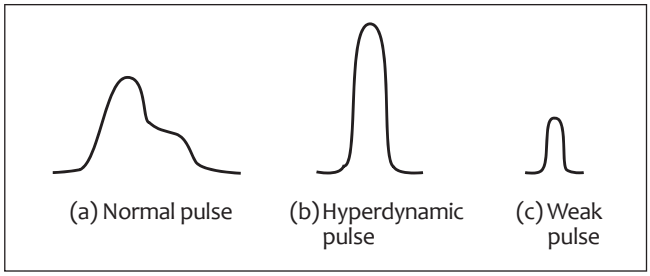
Does the animal require fluid therapy?

Clinical assessment of perfusion status

The perfusion status of the animal should be assessed using mucous membrane colour, capillary refill time (CRT) and vigour, pulse profile (height and width), and heart rate and cardiac auscultation. In uncomplicated hypovolaemia in dogs, the clinical perfusion parameters tend to change in a relatively predictable manner (Figure 4.4). A normal animal should have pink mucous membranes with a vigorous capillary refill, which takes 1–1.75 seconds. A 2 second CRT is often prolonged in the setting of a veterinary clinic. Pulses (femoral and metatarsal) should be carefully palpated to allow assessment of both the height or amplitude (to estimate pulse pressure) and the width or duration of the pulse. Assessment of both the height and width of the pulse allows estimation of pulse volume and, with careful palpation, a perceptive clinician can generate a mental image of the pulse profile (Figure 4.5).

Clinical sign	Mild (compensatory)	Moderate	Severe (decompensatory)
Heart rate	130–150 bpm	150–170 bpm	170–220 bpm
Mucous membrane colour	Normal to pinker than normal	Pale pink	White, grey or muddy
Capillary refill time	Vigorous, <1 second	Reduced vigour, 2 seconds	>2 seconds or absent
Pulse amplitude	Increase	Moderate decrease	Severe decrease
Pulse duration	Mild decrease	Moderate decrease	Severe decrease
Metatarsal pulse	Easily palpable	Just palpable	Absent

4.4 Guidelines for the clinical assessment of uncomplicated hypovolaemia in the dog.



4.5 Pulse profiles from direct arterial pressure measurement. Assessing the height and width of the pulse together allows an estimation of pulse volume. (Note that in practice it is not always possible to palpate the plateau in the normal pulse profile; see Chapter 3.)

An awareness of the normal pulse profile facilitates a meaningful assessment of changes in pulse profile in sick patients. A normovolaemic animal that is stressed or in pain will have a slightly taller and narrower pulse profile than a resting animal. The vast majority of unstressed dogs have a heart rate of 80–120 beats per minute (bpm) in the setting of an emergency clinic, which is unrelated to the dog's bodyweight (Ferasin, Ferasin and Little, 2010).

Clinical assessment of perfusion in cats is more challenging. Normal heart rate in cats usually varies from 170–200 bpm in the veterinary clinic, although this probably represents a moderate tachycardia compared with resting heart rate at home. Mucous membranes in normal cats are significantly paler than in dogs and, although it is possible, it is much more difficult to appreciate the pulse profile in a cat. Critically ill feline patients also tend to develop an inappropriate bradycardia (heart rate in the 130–150 bpm range) despite the presence of hypovolaemic or distributive shock, further complicating their assessment (Brady *et al*., 2000).

In the compensatory stages of uncomplicated hypovolaemia, dogs develop a moderate tachycardia of 130–150 bpm. This increase in rate along with the reduced blood volume and increase in cardiac contractility produces a pulse that is narrower and taller than normal (Figure 4.5b). This pulse will also be narrower than the pulse profile of a normovolaemic dog with tachycardia secondary to stress/exercise or pain. This pulse profile is often referred to as 'bounding' or 'snappy', but these terms often serve to confuse rather than clarify. In compensatory hypovolaemia, metatarsal pulses should still be palpable. Mucous membranes should be pink to pinker than normal with a rapid CRT of less than 1 second duration.

The increases in heart rate seen in dogs with hypovolaemia are surprisingly independent of bodyweight, such that severe hypovolaemia results in a heart rate of 170 to 220 bpm regardless of size. Heart rates in excess of this range should raise suspicions of a primary dysrhythmia rather than a physiological sinus tachycardia in response to hypovolaemia. Heart sounds are sometimes quiet when there is severe hypovolaemia. Mucous membranes have little or no red coloration (white, muddy or grey) and the CRT is prolonged or absent. Femoral pulses are extremely weak (Figure 4.5c) (sometimes referred to as 'thready') and metatarsal pulses are not palpable. While clinically assessing perfusion, the findings should be continually cross-referenced. For example, in a recumbent patient with very weak femoral pulses, pale mucous membranes and a prolonged CRT, the heart rate should be approximately 180–220 bpm. An inappropriately low heart rate should prompt a search for the underlying reason, such as hyperkalaemia associated with postrenal, renal or endocrine causes.

Lactate

Tissue hypoperfusion results in increased lactate production and decreased removal of lactate, and blood lactate concentration can be used to assess the severity of hypovolaemia. The reference value for plasma lactate concentration in normal dogs by direct amperometry is <2.5 mmol/l, irrespective of sample site. A blood lactate concentration in the range of 3–4 mmol/l constitutes a mild increase, 4–7 mmol/l is a moderate increase and >7 mmol/l represents a severe increase. Clinical experience suggests that lactate concentration accurately reflects the degree of uncomplicated hypovolaemia in dogs. Furthermore, plasma lactate concentrations almost invariably fall with successful fluid resuscitation and can be used to guide fluid therapy. Failure of plasma lactate concentration to normalize following fluid resuscitation suggests ongoing systemic hypoperfusion or an occult source of lactate production. Lactate can also be used as a prognostic indicator. In one of the landmark studies in humans, as lactate concentration increased from 2.1 to 8.0 mmol/l, survival decreased from 90% to 10%. There is an increasing body of clinical data suggesting that lactate is similarly associated with prognosis in dogs (Ateca *et al*., 2015; Cortellini *et al*., 2015). If plasma lactate concentration fails to fall following an appropriate fluid challenge, or if a significant and sustained rise in plasma lactate concentration occurs, the prognosis for survival appears to be poor. Lactate also increases with hypoperfusion in cats, although the increase may not be as significant as in dogs with a similar severity of disease and the association with prognosis is less clear (Reineke *et al*., 2015).

Clinical assessment of hydration status

The widely accepted method for determining hydration status involves assessing the moisture of the gums and cornea, skin turgor, presence or absence of retraction of the globe, and perfusion parameters (Figure 4.6). Dryness of the mucous membranes alone is said to reflect dehydration equivalent to 5% of the bodyweight, and >12% dehydration may represent a fluid loss sufficient to cause overt signs of mild to moderate hypovolaemic shock. Interestingly, there is little or no scientific evidence supporting this. When one considers the variable effect on intravascular volume, which depends upon the tonicity of fluid losses and the compartments from which the loss occurs, it is apparent that this scheme allows only a rough approximation of fluid deficits. Bodyweight represents the only easily available, reasonably accurate way of assessing the severity of dehydration, but is rarely relevant immediately following admission as few patients have a known accurate bodyweight from the time immediately before their illness started. Bodyweight can, however, be used as a monitoring tool; dehydrated patients should gain weight following appropriate fluid therapy.

Clinical signs		Dehydration estimate (% of bodyweight)
Normal		<5%
Dry mucous membranes only		5%
Reduced skin turgor	Mild	6–8%
Increased heart rate	Moderate	8–10%
Weak pulses	Severe	10–12%
Collapse, shock		12–15%

4.6 Guidelines for the clinical assessment of dehydration.

The classic scheme will tend to underestimate losses when free water is lost in excess of solute and to overestimate losses of hypertonic fluid. A clinical study performed over 30 years ago (Hardy and Osborne, 1979) found that the clinical signs of dehydration due to free water loss were extremely unpredictable. Of the 20 dogs that were deprived of water for periods ranging from 2 to 4 days, 10 showed no clinical signs of dehydration and no dogs exhibited dry mucous membranes or dry or sunken eyes. One dog deprived of water for 4 days lost 16% of its bodyweight, showed no change in skin turgor, had no change in its packed cell volume (PCV) and a minimal change in total protein concentration.

Despite the limitations of the classic scheme for assessing fluid requirements, it nevertheless provides a tried and tested starting point on which to base chronic fluid replacement therapy. The tendency to underestimate replacement requirements in animals with greater free water loss may actually be appropriate, because these losses tend to be chronic and require more gradual replacement. This scheme should not be used when an animal is showing signs of hypoperfusion; in that situation fluid therapy should be aimed at rapid intravascular volume replacement.

Types of parenteral fluid

Fluids should not be regarded as a single entity; rather, they are a range of pharmacological products, each with its own indications and contraindications, much like the choice of antibiotics for different infections or the selection of heart medications for different types of heart disease. Knowledge of the underlying disease processes and assessment of fluid deficits will help to determine the most appropriate fluid. There are three main groups of fluids:

- Crystalloids – electrolyte solutions that can pass freely out of the vascular space
- Colloids – contain macromolecules that are retained within the vascular space for a longer time period than crystalloids
- Blood products – covered in more detail in Chapter 14.

Crystalloids

Crystalloid fluids can be hypotonic, isotonic or hypertonic (Figure 4.7) compared with extracellular (and therefore intracellular) fluid. The tonicity of the solution will determine its distribution following intravenous infusion (Figure 4.8).

Isotonic solutions

Isotonic replacement crystalloid solutions are the most familiar and frequently used fluid group in small animal veterinary medicine. They are tremendously versatile fluids and can be used (at different rates) to treat both hypovolaemia and dehydration, and to support the patient with ongoing losses. The most widely available isotonic replacement fluids are normal (0.9%) saline, Ringer's solution and Hartmann's solution (lactated Ringer's solution). When used to treat hypovolaemia, there is no concentration gradient change between the intracellular and extracellular spaces, therefore water shifts do not occur across the cell membrane (Figure 4.8c). Intravascular crystalloid equilibrates with the interstitial space, with 20–25% of the infused volume remaining within the intravascular space 1 hour following infusion.

Isotonic replacement crystalloids have an electrolyte composition similar to extracellular fluid, with a relatively high sodium and low (or zero) potassium concentration (see Figure 4.7). Consequently, when used for longer-term fluid therapy, there is a tendency for patients to develop hypokalaemia and have a mild increase in their serum sodium. Whilst the change in sodium is rarely of clinical significance, if the patient has limited intake of potassium from other sources (e.g. is anorexic) the decrease in serum potassium may be significant. Supplementation of the intravenous fluids with potassium should be considered once acute volume deficits have been replaced (see Chapter 5).

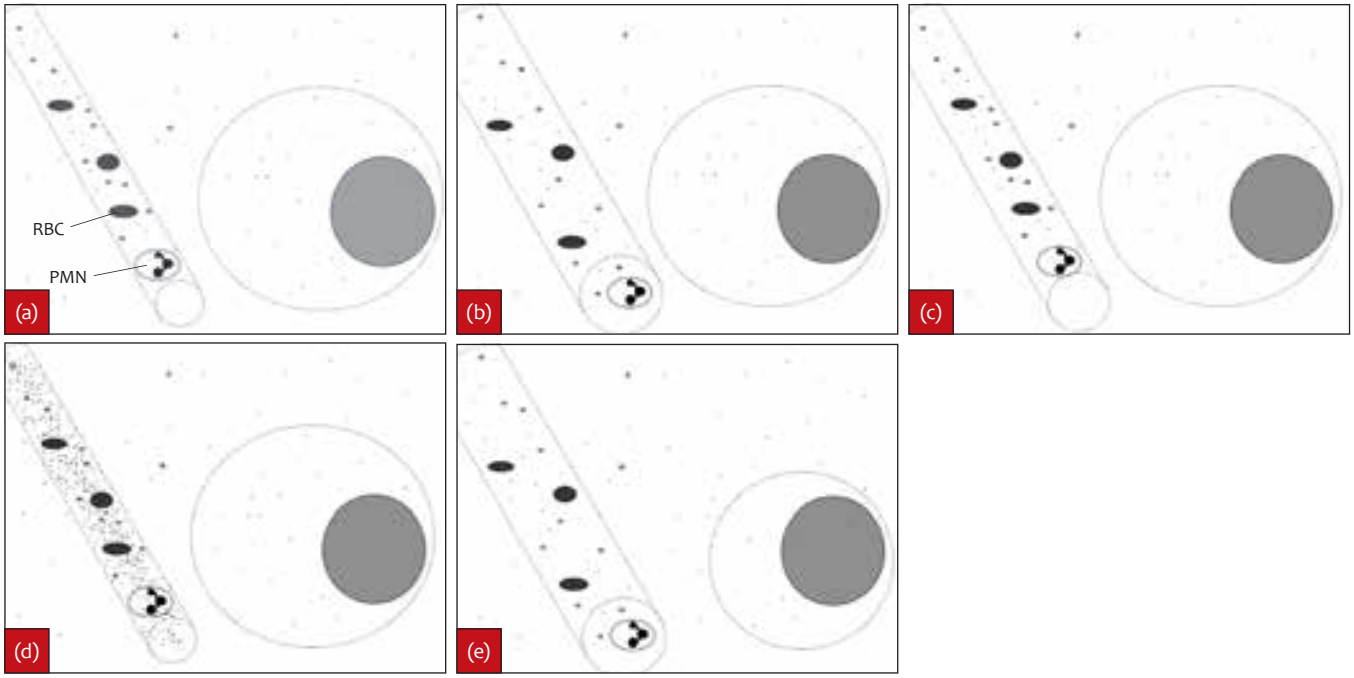
Alternatively, isotonic maintenance fluids can be used. These fluids have an electrolyte composition that more closely mimics the electrolytes lost due to insensible causes in a healthy animal. As these fluids have a relatively high potassium concentration (see Figure 4.7), they must only be used at slow rates (e.g. 2 ml/kg/h). Due to their lack of versatility and the small number of patients for which their use is indicated, they are rarely used in veterinary practice.

Hypertonic saline

Hypertonic saline is most commonly supplied at a concentration of 7.2–7.5%, which, at approximately 2400 mOsm/l, is more than eight times the concentration of plasma. A dosage of 4–7 ml/kg (dogs) or 2–4 ml/kg (cats) is given over 2–5 minutes, and produces a haemodynamic response similar to that of an isotonic crystalloid dose of 60–90 ml/kg. Intravenous infusion of a hypertonic crystalloid creates a large osmotic gradient (Figure 4.8d) and water is drawn from the interstitial and intracellular compartments, producing a rapid expansion of intravascular volume (Figure 4.8e).

Name of fluid	Description of fluid (*in vivo* tonicity)	Na^+ (mmol/l)	K^+ (mmol/l)	Cl^- (mmol/l)	Ca^{2+} (mmol/l)	Osmolality (mOsm/l)	pH
Hartmann's (lactated Ringer's) solution	Isotonic replacement	131	5	111	2	272	6.5
NaCl 0.9%	Isotonic replacement	150	0	150	0	308	5
Ringer's solution	Isotonic replacement	147	4	155.5	2.25	310	5.5
NaCl 0.9% + glucose 5%	Isotonic replacement	150	0	150	0	560	4
NaCl 0.45%	Hypotonic	77	0	77	0	154	
NaCl 0.18% + glucose 4%	Hypotonic	30	0	30	0		
Glucose 5%	Hypotonic	0	0	0	0	252	
NaCl 7.2%	Hypotonic	1232	0	1232	0	~2400	
Plasma-lyte M	Maintenance	40	16	40	2.5		

4.7 Composition of crystalloid fluids for intravenous administration.



4.8 (a) Hypovolaemic shock. Large open dots represent albumin molecules and small dots represent small solutes. (b) Intravascular expansion during infusion of isotonic crystalloid. There is no concentration gradient change between the intracellular and extracellular space. (c) Intravascular expansion with isotonic crystalloid. Intravascular crystalloid equilibrates with the interstitial space and intravascular volume falls compared with the initial volume of expansion. (d) Intravascular expansion following hypertonic crystalloid results in a large increase in intravascular sodium concentration and a large osmotic gradient for water to flow into the vasculature. (e) Intravascular expansion following hypertonic crystalloid. Water passes into the intravascular space from the interstitial and intracellular compartments, producing a rapid, but transient, expansion of intravascular volume. PMN = polymorphonuclear leucocyte ; RBC = red blood cell. The major extracellular cation is sodium (○) and the major intracellular cation is potassium (●). Small dots represent water molecules.

However, as the sodium rapidly diffuses out of the vasculature, the effects can begin to wane in as little as 30 minutes following infusion. To prolong the duration of effect, hypertonic saline may be constituted with a colloid.

Hypertonic solutions have been reported to be safe and effective for the treatment of hypotension in experimental studies in a wide range of species including dogs and cats. When compared with crystalloid solutions alone, many potential benefits have been demonstrated, including:

- Cardiovascular effects
  - Improved cardiac output
  - Arteriolar (including coronary) vasodilation
  - Possible weak inotropic effect
  - Improved cerebral perfusion pressure by increasing mean arterial pressure whilst concurrently reducing intracranial pressure
- Immunomodulatory effects
  - Suppression of neutrophil respiratory burst activity
- Other
  - Reduced endothelial swelling
  - Reduction in organ damage following resuscitation
  - Lower total volume of resuscitation fluid required
  - Reduction in time taken for resuscitation.

Clinical indications: Hypertonic saline is extremely useful when rapid intravascular volume expansion is required, such as the occasional case of severe hypovolaemia when death is imminent. It is also useful in large-breed dogs and in hypovolaemic animals in which inappropriately small intravenous catheters have been placed. Hypertonic saline may be the fluid of choice in patients with head trauma and hypovolaemia representing the best compromise between improving the arterial blood pressure and minimizing the increase in intracranial pressure (i.e. optimizing cerebral perfusion pressure).

Contraindications:

Dehydration and hyperosmolality: Animals suffering from dehydration do not have a normal reservoir of interstitial and intracellular fluid for mobilization following infusion of hypertonic saline. Similarly, use of hypertonic saline may be contraindicated in animals with hypernatraemia or other hyperosmolar states. Administration of hypertonic saline may also lead to hypernatraemia, although usually this is of no clinical significance unless repeated doses are used or the animal has pre-existing electrolyte abnormalities.

Volume overload: Hypertonic resuscitation is sometimes referred to as small volume resuscitation. However, this should not lead to the mistaken assumption that the effects on the cardiovascular system are also small. Volume expansion with hypertonic saline is a very rapid and aggressive method of fluid resuscitation irrespective of the small volume infused. It should be avoided or used with extreme caution in patients in which aggressive volume expansion would be dangerous, such as patients with heart or lung disease.

Ventricular dysrhythmias: Hypertonic saline may cause ventricular dysrhythmias, especially when given rapidly, therefore an electrocardiogram should ideally be monitored during infusion.

Uncontrolled haemorrhage: Experimental evidence and clinical experience support the view that aggressive volume expansion in patients with uncontrolled haemorrhage is associated with a higher mortality rate. This is probably due to an increase in the volume of haemorrhage and loss of red blood cells, platelets and clotting factors following aggressive volume expansion. However, there are also studies documenting increased mortality following hypertonic saline resuscitation, even after changes in blood pressure

and volume of haemorrhage are taken into account. The most common situation in which uncontrolled haemorrhage is encountered in clinical small animal practice is following road traffic accidents. Intra-abdominal haemorrhage and pulmonary contusions are the most common sites of bleeding. Notably, pulmonary bleeding appears to be exquisitely sensitive to volume expansion. Aggressive fluid resuscitation, such as with hypertonic saline, almost always worsens pulmonary bleeding and the authors consider the use of hypertonic saline, or any form of aggressive volume expansion, to be contraindicated in this patient population.

Hypotonic solutions

Hypotonic solutions include:

- 5% glucose (D5W)
- 0.18% NaCl + 4% glucose
- 0.45% NaCl.

Although the osmolality of 5% glucose solution is 252 mOsm/l (and thus in the fluid bag it is close to being isotonic), once administered to the patient, the glucose is rapidly taken up by cells and metabolized. Administering glucose solutions is therefore tantamount to giving free water (i.e. water without associated solute). Free water rapidly passes out of the intravascular space and distributes across the total body water, thus it is an ineffective intravascular volume expander and should not be used for the treatment of hypoperfusion. Furthermore, rapid infusion of hypotonic solutions can cause severe dilution of serum electrolytes, especially sodium, and result in acute cerebral oedema and death. Although there are rare uses for hypotonic fluids (e.g. in patients with severe hypernatraemia), their use is contraindicated in most situations.

Artificial colloids

The theoretical basis for the use of colloids for volume expansion, as opposed to crystalloids, is that they are retained in the intravascular space to a greater degree than crystalloids and are therefore more efficient in maintaining intravascular volume. As long as microvascular permeability is normal, colloids will also maintain the intravascular COP and the COP gradient between the intravascular and interstitial spaces, thereby reducing the rate of fluid efflux from the vasculature. Experimental studies confirm that the ratio of colloids:crystalloids needed to achieve a similar volume effect is approximately 1:4 (Silverstein *et al*., 2005). As such, they may seem like a logical choice for volume expansion. However, they are also associated with a num-ber of known adverse effects as described below. Furthermore, recent evidence from human clinical patients suggests that the actual volume expansion effect may be much lower than anticipated from the experimental studies, with a colloid:crystalloid ratio of 1:1 to 1.58. This discrepancy is thought to be due to damage to the endothelial glycocalyx that occurs in many critical illnesses. Recent meta-analyses in human medicine failed to find any evidence that resuscitation with colloids of any type leads to an improvement in mortality and found some evidence that the use of hydroxyethyl starch products may be associated with a worse outcome (Perel *et al*., 2013). Specifically relating to hydroxyethyl starch solutions, several large randomized controlled clinical trials have demonstrated a higher incidence of acute kidney injury, need for renal replacement therapy, and number of blood transfusions in patients resuscitated with hydroxyethyl starch products as opposed to crystalloids (Brunkhorst *et al*., 2008; Myburgh *et al*., 2012; Perner *et al*., 2012). Current guidelines for use in human critical care such as the Surviving Sepsis Guidelines advise against the use of hydroxyethyl starch in sepsis and septic shock, as does the European Medicines Agency. Although similar studies are not available for small animal patients, a high degree of caution is recommended when considering colloid use.

Types of artificial colloid

There are three common types of artificial colloid: the gelatins, the dextrans and the hydroxyethyl starches (Figure 4.9). Gelatins are produced from mammalian collagen, whereas dextrans are prepared from a macromolecular polysaccharide produced from bacterial fermentation of sucrose. Hydroxyethyl starches are derived from amylopectin (the branched form of plant starch). The parent mixtures of macromolecules are separated into fractions according to molecular weight. Artificial colloids contain a mixture of molecules of varying weights (i.e. are polydisperse), with the hydroxyethyl starches having a much wider range of molecular weights than dextran 70 or the gelatins. Albumin, by comparison, is a monodisperse colloid, with molecules that are all the same size (molecular weight 69 kD, molecular radius 3.5 nm). An average molecular weight of 100–300 kD would seem to be ideal, providing the best compromise theoretically between colloid osmotic volume expansion and duration of action. Mean molecular weights of the commonly available colloids are shown in Figure 4.9.

In addition to their weight, hydroxyethyl starches are also described by their degree of molar substitution. To reduce intravascular hydrolysis of the hydroxyethyl starch by amylase, the amylopectin may be hydroxyethylated at carbons 2, 3 and 6. The number of hydroxyethyl groups per glucose unit is defined as the molar substitution ratio. The pattern of substitution varies depending upon the synthetic process. Substitution at the carbon 2 position is more effective at reducing intravascular hydrolysis than hydroxyethylation at the other positions. Hydroxyethyl starches can therefore be described on the basis of their average molecular weight, degree of substitution and C2/C6 hydroxyethylation ratio. These factors can be used to predict their intravascular persistence and their potential effect on coagulation (see below).

Type of colloid	Fluid name	Mean molecular weight (kD)	Degree of molar substitution	COP (mmHg)	Na^+ (mmol/l)
Gelatin	Gelofusin®	35	–	~25	154
Dextran	Dextran 70	70	–	62	150
Hydroxyethyl starch	Hetastarch 6% in 0.9% NaCl	450	0.7	33	154
Hydroxyethyl starch	Pentastarch 6% in 0.9% NaCl	200	0.5	36	154
Hydroxyethyl starch	Tetrastarch Voluven® (6% in 0.9% NaCl)	130	0.4	~30	154

4.9 Description of colloid fluids. It should be noted that Haemaccel also contains calcium and must not be administered with blood products. A 10% solution of Pentastarch (HAES-steril®) is also available.

The effect (both magnitude and duration of action) of colloids may be measured in several ways, including assessment of plasma colloid concentrations, plasma COP and intravascular volume expansion. These parameters do not change in an identical way following infusion of a colloid. The initial volume of intravascular expansion is due to the colloid osmotic pressure of the infused colloid, which is determined by the number of molecules and not their size. Smaller molecules, which are responsible for a large part of the COP and intravascular volume expansion, are excreted or extravasated within hours. The larger molecules remain in circulation and are enzymatically degraded or removed by the monocyte phagocytic system. The rapid initial excretion of small, osmotically active molecules, followed by a gradual elimination of large molecules, results in an exponential decline in intravascular expansion and a narrowing of the distribution of molecular weights. Because the larger molecules persist longer than the smaller ones, the concentration (i.e. the mass per unit volume) will remain high; however, as the total number of molecules decreases very quickly, the COP will decrease more rapidly. In summary, the COP and degree of volume expansion tend to fall faster than the plasma concentration of colloid. Studies that report the pattern of volume expansion are therefore most applicable to the clinical situation.

Many factors influence the volume and duration of intravascular expansion associated with artificial colloids, including the species of animal, the dosage, the specific colloid formulation, the pre-infusion intravascular volume status and the microvascular permeability. It should be apparent that data from an experimental study in normovolaemic human volunteers given twice the usual dose of a low molecular weight form of hydroxyethyl starch may have little bearing on the effects of hydroxyethyl starch in a dog with SIRS that is in hypodynamic septic shock.

It should be noted that gelatins, which have a veterinary licence in the UK, have a shorter duration of action than the other colloids because of their smaller molecular size. Following infusion over a 90 minute period, intravascular expansion with polygeline was only 24% of the infused volume. For comparison, on average 20–25% of the infused volume of crystalloid remains in the intravascular space 1 hour following infusion. As colloids are most commonly used in the most critical patients when it is impossible to predict the degree of effect, it is vital that all patients are monitored to evaluate the clinical effect of the dose and product chosen in the individual patient.

Indications

The popularity of artificial colloids has varied over the years and in veterinary medicine, where large-scale randomized controlled clinical trials are not yet available, is still largely informed by the individual clinician's opinion and experience. Whilst improvements have been made to the safety profile of the hydroxyethyl starch products, particularly with relation to coagulopathy, the recent evidence from human clinical trials, relating to incidence of acute kidney injury, is of concern. Further, the evidence relating to efficacy, in terms of their volume expansion effects in clinical patients, means the rationale for their use is also increasingly questionable. Whilst direct extrapolation of results between species may not be accurate, when considering whether to use colloids for the indications discussed below, it is important clinicians are also aware of the potential risks. The authors now very rarely use artificial colloids in clinical practice.

Volume expansion: In some patients, colloids may be an efficient means of intravascular volume expansion. However due to the concerns over safety, they are generally only recommended for use when crystalloid fluids (isotonic or hypertonic) are considered to be insufficient. Because the osmotic effect of the colloid macromolecules is due to their number rather than their size, if more than 50% of the molecules leak into the interstitium, then there could theoretically be a net reduction in intravascular volume and a worsening of interstitial oedema as water leaves the intravascular space along with colloid. The dilemma therefore becomes the estimation of the increase in capillary permeability, i.e. the size of the 'gaps' in the microvascular barrier.

Hypoproteinaemia: Although colloid fluids may be considered for use in hypoproteinaemic patients with the aim of raising COP, this rationale is no longer sound due to our better understanding of the minimal role COP plays in transvascular fluid flux. This means that a low plasma COP per se does not necessitate colloid therapy in the absence of clinical signs such as hypovolaemia or oedema. Indeed, humans with a hereditary form of complete albumin deficiency have a plasma COP that is still half of normal due to elevated globulin levels, and affected individuals exhibit minimal peripheral oedema. There also appear to be no serious clinical signs in an autosomal recessive, hereditary albumin deficiency reported in rats. In the authors' clinical experience and in experimental studies, animals with severe hypoproteinaemia (COP <11 mmHg) may exhibit peripheral oedema but rarely develop pulmonary oedema. It is more important to diagnose and treat the cause of the hypoproteinaemia, rather than to administer palliative colloid therapy, which is unlikely to be successful for more than a few hours if the underlying cause is not corrected.

Contraindications and side effects

Acute kidney injury: A number of recent studies have documented a higher incidence of acute kidney injury and need for renal replacement therapy in human patients resuscitated with artificial colloid fluids (Brunkhorst *et al*., 2008; Myburgh *et al*., 2012; Perner *et al*., 2012). Evidence is emerging that similar risks exist in our clinical patients (Hayes *et al*., 2016) and the low molecular weight dextrans have been reported to cause renal dysfunction in experimental dogs.

Vascular leak states: The balance of current evidence is convincing that the use of artificial colloids in vascular leak states are associated with higher mortality in people even when disease severity has been taken into account. The Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016 recommend against using hydroxyethyl starches (HESs) for intravascular volume replacement in patients with sepsis or septic shock (strong recommendation, high quality of evidence). The guidelines also suggest using crystalloids over gelatins when resuscitating patients with sepsis or septic shock.

The deleterious effects of colloids in vascular leak states include: 1) extravasation resulting in interstitial and intracellular accumulation of colloids causing dysfunction; 2) interference with cell to cell recognition and adhesion molecules that are especially important in immunity and coagulation; and 3) colloid-induced renal injury.

Coagulopathy: Coagulopathy is one of the most common side effects associated with artificial colloids. Deleterious effects on coagulation can occur when high molecular

weight hydroxyethyl starches or dextran are administered at doses above 20 ml/kg/day. Novel colloid solutions such as the tetrastarches were designed to reduce these effects and may be used at up to 50ml/kg/day. The important question is whether these coagulopathies are clinically significant. Some studies suggest that clinically significant haemorrhage does not occur; however, there is also clinical and experimental evidence suggesting occasional serious, potentially life-threatening bleeding. This paradox means simply that the coagulation abnormalities are clinically significant in only some cases. Clinical experience suggests that bleeding complications are relatively uncommon in veterinary patients. The effects on coagulation appear to be directly related to the intravascular concentration of artificial colloid and the molecular weight and molar substitution of the molecule itself. Higher plasma concentrations of colloid may occur following larger doses, repeated administration or reduced intravascular degradation. Larger colloid molecules have a greater effect on coagulation than small molecules. With repeated administration, the small molecules are constantly excreted and the relative concentration of larger molecules increases. This explains why many studies reporting clinically significant bleeding refer to patients who received repeated administration over a period of days. The exact mechanism of action by which coagulation is affected is still not fully understood. The most repeatable findings are a reduction in factor VIII and von Willebrand factor (greater than expected by dilution alone), weakened clot formation, and impairment of platelet function.

Volume overload: Colloids are retained within the vasculature to a greater extent than crystalloids; therefore there is a greater likelihood of volume overload with injudicious administration. Particular care must be taken in patients with concurrent issues making them susceptible to volume overload such as cardiac or pulmonary disease or oliguria.

Allergic reactions and reticuloendothelial dysfunction: Anaphylactic or anaphylactoid reactions have been reported for dextrans, hydroxyethyl starches and gelatins; however, the incidence of serious complications is extremely low. Hydroxyethyl starch has been associated with pruritus in up to one-third of humans treated with long-term infusions. Deposits of hydroxyethyl starch in cutaneous nerves and histiocytic skin infiltrates are thought to be responsible. Several studies have raised concerns regarding the potential effects of plasma substitutes on reticuloendothelial function. Decreased concentrations of the opsonic plasma factor, fibronectin, have also been reported. These appear to be most significant with the artificial gelatins but have also been noted with hydroxyethyl starch.

Interference with clinical biochemistry: The use of refractometric total solids (TS) as a convenient and cheap way to assess total protein concentrations and estimate COP is no longer valid once an artificial colloid has been administered. High molecular weight hydroxyethyl starch and dextran 70 both yield refractometric TS of 45 g/l. As plasma volume is replaced by artificial colloid, theoretically the measured refractometric TS should tend towards that of the artificial colloid. In clinical patients, administering artificial colloid to an animal with an initial TS >45 g/l will tend to reduce the measured TS despite the fact that it will lead to an increase in COP. However, it is rare that administration of artificial colloid will cause a significant increase in TS if the initial TS is <45 g/l. Failure to appreciate the effect of artificial colloid on refractometric TS can lead the clinician to misinterpret a fall in TS as an indication for more colloid. Because assays for serum colloid concentrations are not readily available, therapy with artificial colloids is best monitored by direct measurement of COP using a membrane osmometer.

The intravascular expansion due to colloid infusion results in significant dilutional effects. PCV, albumin concentration and serum potassium concentration seem to be most affected. Serum amylase may be elevated to 200–250% of normal following administration of hydroxyethyl starch due to complex formation and reduced excretion. Hydroxyethyl starch can also produce predictable but potentially misleading results in blood typing and cross-matching, due to increased rouleaux formation.

Urine specific gravity (USG) should be interpreted with caution following colloid administration. As many of the colloid molecules are excreted through the kidneys and as USG is a measure of the weight of solutes in urine, the USG may increase without representing an increase in urine concentrating ability.

Natural colloids

Until recently, albumin has been administered to small animal patients only in veterinary transfusion products (see Chapter 14). Canine plasma products may be used as an initial resuscitative fluid; however, considering the volumes likely to be required, this rarely occurs due to cost. Human serum albumin (HSA), obtained from purified human plasma, is available commercially and has been used in small animal medicine. Canine serum albumin can be produced from canine plasma products but is only available currently in certain states of the USA and not in Europe. Albumin is a monodisperse colloid (i.e. all albumin molecules are the same size) with a molecular weight of approximately 69 kD and a molecular radius of 3.5 nm. In addition to its role in maintaining plasma COP, it is also a carrier molecule, with a wide range of substances being bound to it in plasma (e.g. bilirubin, fatty acids, metals and other ions, hormones and drugs). Albumin supplementation has been suggested in critically ill people because of its numerous important roles, and because serum albumin concentration has been shown to be an accurate prognostic indicator. The role of albumin in maintaining the selective permeability of the microvascular barrier to macromolecules provides another rationale for the prophylactic use of albumin. As albumin is concentrated into the glycocalyx, there may be a role for low-dose fresh frozen plasma (FFP) in maintaining the selective permeability of the microvascular barrier. HSA is currently one of the most used colloids in human critical care, although there is no clear evidence of a significant benefit over crystalloids alone. Use of HSA in small animal clinical patients has been described (Trow *et al*., 2008; Vigano *et al*., 2010) however, as human albumin is not biochemically identical to canine albumin there is a risk of both immediate and delayed side effects. A fatal hypersensitivity reaction has been reported in a healthy dog (Cohn *et al*., 2007). HSA should only be used with great caution when other options have been exhausted and with appropriate informed owner consent.

Frozen or fresh frozen plasma remains a relatively accessible source of canine albumin. When considering its use as a volume expander, it must be remembered that as the albumin molecule is relatively small, it equilibrates with the interstitial space more rapidly and to a greater extent than the larger artificial colloids. Thus, relatively large

volumes must be given to achieve a sustained increase in plasma albumin concentration and intravascular volume. The amount of albumin required can be estimated using an equation that corrects for the expected volume of distribution across the intravascular and interstitial spaces:

Albumin deficit (g) = (desired albumin (g/l) – patient albumin (g/l)) x (bodyweight (kg) x 0.3)

Therefore, to raise the serum albumin from 15 to 25 g/l in a 20 kg dog:

Albumin deficit = (25 – 15) x (20 x 0.3) = 60 g

This would be equivalent to the amount of albumin in 2 l of plasma or 4 l of fresh whole blood.

Volume, rate, duration and route of administration of fluid therapy

Acute intravenous fluid therapy to replace absolute or relative plasma volume deficits in a patient with hypoperfusion is a life-saving procedure that must be performed over minutes to hours. In contrast, chronic fluid therapy to re-establish and maintain normal water, electrolyte and acid–base balance is not usually an emergency response and is planned and re-evaluated on a daily basis. It is vital to separate the doses and rates used for acute volume expansion from the rates used for chronic fluid therapy to ensure that life-threatening problems are corrected in a timely manner. In many situations there is more than one fluid type that could be used and the clinician must consider the relative indications and contraindications of each fluid in that particular patient.

It is also important to remember that all fluid therapy calculations are based on estimates. Successful fluid therapy relies on monitoring the patient closely to ensure that appropriate goals are being achieved, with adjustment of the plan if necessary. Goal-directed fluid therapy, where the volume of fluids administered is decided upon on the basis of achieving specific measurable endpoints, is now widely considered to be best practice (Rhodes *et al*., 2017). For all patients receiving fluid therapy, the clinician should ask 'What do I want the fluids to achieve in this patient?' and 'Are there contraindications to the use of any fluid groups in this patient?' Once these questions are answered, the clinician makes a decision on the initial type and dose/rate of fluid to be administered and the parameters to be monitored, both to check that the fluids are having the required effect and to ensure that no complications of fluid therapy develop. If the patient is not responding as expected, the clinician should re-evaluate the fluid plan, including both the type and rate of fluids.

Acute fluid therapy for the animal with perfusion abnormalities

To determine the appropriate fluid dosage, abnormalities of perfusion should be graded as to their severity (see Figure 4.4). A bolus dose (ml/kg) of fluid should then be chosen and administered over a defined time frame with the aim of restoring intravascular volume (and therefore perfusion parameters) to within normal limits without giving excessive amounts that would contribute to formation of interstitial oedema. A positive fluid balance has been associated with a worse outcome in humans (Boyd *et al*., 2011) and regular (15 minute) reassessments are recommended in all patients receiving fluid boluses to try and optimize the balance of restoring perfusion without administering excess fluid. Considering isotonic crystalloids, a full 'shock' dose is approximately equivalent to a blood volume at 60–90 ml/kg (dog) and 40–60 ml/kg (cat). This is rarely given as a single bolus, particularly in cats, with the exception being dogs exhibiting signs of imminently life-threatening hypovolaemia. More commonly in patients with signs of moderate to severe hypoperfusion, a 25–50 ml/kg bolus should be used (10–20 ml/kg in the cat) and for patients with signs of mild hypoperfusion a smaller bolus of 10–20 ml/kg (5–7 ml/kg in the cat) should be chosen. The fluid dose should be administered over a defined time frame (usually 30 minutes–1 hour), although in dogs with severe hypoperfusion it may be necessary to administer the dose more rapidly. At the end of the dose the patient's perfusion parameters should once again be assessed. If they are within normal limits, fluid therapy should continue to replace ongoing losses, with doses as outlined in the chronic fluid therapy plan described below. In contrast, if perfusion parameters are still abnormal, another fluid bolus should be given.

Hypotensive resuscitation is a concept that may be considered in patients with hypovolaemia secondary to acute haemorrhage or in patients with alveolar lung disease. In this scenario, rather than administering fluid therapy to achieve the endpoint of normal systolic blood pressure, fluids are used until systolic blood pressure is slightly lower than the normal range (i.e. aiming for a systolic blood pressure of 80–90mmHg). This strategy theoretically reduces blood loss whilst preserving blood flow to vital organs and is supported by some experimental and human clinical literature (Carrick *et al*., 2016). Its place in clinical veterinary medicine is as yet unknown; it is important to remember that it is only a temporary strategy to be used in the time between presentation and definitive control of the bleeding, usually by surgical intervention.

Prior to administering aggressive fluid therapy, a careful assessment should be made of possible reasons for the hypoperfusion and whether there are any contraindications to rapid fluid therapy. The vast majority of animals with poor perfusion have hypovolaemia, distributive shock (sepsis or other causes of SIRS) obstructive, or less commonly cardiogenic shock (see Chapter 3). Fluids are essential in the treatment of both hypovolaemic and distributive shock but contraindicated in most animals with cardiogenic shock. Most animals with significant heart disease as a cause of their shock will have a murmur or gallop rhythm on cardiac auscultation. However, in patients with severe hypovolaemia, the heart sounds can be quiet, making it challenging to auscultate concurrent cardiac abnormalities. The major contraindications to aggressive fluid therapy are cardiac, respiratory or brain disease. Although anuric renal failure also warrants careful fluid therapy, it is impossible to confirm this diagnosis without an appropriate fluid challenge.

Fluids for acute intravascular volume replacement should always be given by the intravenous or intraosseous route. Flow rate through a catheter is proportional to the fourth power of the radius of the catheter, thus the largest bore possible should be used (see Chapter 2). It is often helpful to place two intravenous catheters to ensure that an adequate fluid volume can be administered and to provide a back-up if one catheter does not flow or becomes dislodged. In animals with severe hypoperfusion surgical venous cut-downs may be necessary to establish venous access (see Chapter 2).

Animals receiving intravenous fluids for rapid intravascular volume expansion should be constantly monitored to assess the clinical response to therapy. In general, during successful volume replacement, perfusion parameters will gradually and predictably return to normal. Mental status should improve and there should be no deleterious effects on the respiratory system. Given a dog of a certain bodyweight with a given degree of hypovolaemia, the expected clinical response from a given volume and type of intravenous fluid can be estimated. This enables the clinician to detect an inadequate response to volume resuscitation rapidly and pursue the underlying cause (e.g. ongoing haemorrhage, sepsis/SIRS). The fluid type and rate should be reassessed, as patients with severe ongoing losses may require blood component therapy.

Although isotonic replacement crystalloids are often the first choice in the fluid resuscitation of patients in shock, blood products or hypertonic saline may also be chosen. Blood products should be considered if the patient has pre-existing anaemia or has experienced severe haemorrhage, but their immediate use is often limited by practicality and they are more commonly used to follow on from initial crystalloid resuscitation. Fluid resuscitation with asanguineous fluids should rarely if ever be withheld due to concerns about decreased red cell mass. Hypertonic saline should be considered in patients with concurrent hypovolaemia and head trauma or in large patients in severe shock. Colloids are rarely used as the initial resuscitative fluid but may be considered if resuscitation with crystalloid fluids is unsuccessful. A colloid dose of 20 ml/kg is considered equivalent to a 60–90 ml/kg dose of isotonic crystalloid, and the dose should be scaled down according to the severity of shock in the same manner as described for crystalloids.

Chronic fluid therapy for the patient with normal perfusion parameters

If the patient's perfusion parameters are within normal limits (either at presentation or following correction of shock with acute fluid therapy as described above), a chronic fluid therapy plan should be formulated. For the animal that is dehydrated but not hypovolaemic, it is appropriate to correct fluid, electrolyte and acid–base abnormalities over a period of 24–48 hours. When devising a chronic fluid therapy plan, three components should be considered:

- Pre-existing fluid deficits (replacement of hydration losses)
- Maintenance requirements
- Ongoing losses.

The volume of fluids required for replacement of dehydration is estimated as a percentage of the animal's bodyweight, based on the clinical signs of hydration status (see Figure 4.6). As discussed previously, this provides only a rough estimate rather than an accurate guide. Because of the need to expand the intravascular and interstitial compartments effectively, an isotonic fluid is used for replacement of pre-existing deficits. Maintenance fluid requirements are simply the water and electrolytes needed on a daily basis in a normal animal. They are estimated empirically at 60 ml/kg/day for small dogs and cats and 40 ml/kg/day for larger dogs. In general, the fluid composition required for maintenance is low in sodium (approximately 0.3–0.45% NaCl) and high in potassium (approximately 20 mmol/l). Ongoing losses should also be estimated, although occasionally they may be measured (e.g. losses via a chest tube by collecting drainage or losses in diarrhoea by weighing soiled bedding). Increased insensible losses, such as panting (especially with pyrexia), can be significant and should be taken into account when planning ongoing requirements.

In practice, replacement isotonic crystalloids are used for the chronic fluid therapy plan, as most patients still have some degree of replacement needs or ongoing losses. The use of replacement fluids in this situation tends to predispose patients to the development of hypokalaemia. Patients that have only maintenance requirements (e.g. the neurological patient with inability to drink) are rarely encountered. In this situation, a maintenance fluid may be used, although the use of a replacement solution with potassium supplementation is also likely to be successful.

In animals that require potassium supplementation, an empirical dose is usually added to the intravenous fluids (see Chapter 5). In very small patients or those on rapid fluid rates, the potassium infusion rate should be calculated to double check that the patient is not being overdosed. An empirical maximum infusion rate of 0.5 mmol/kg/h is suggested for potassium. The converse also should be kept in mind: the standard potassium supplementation of fluids may be insufficient to correct plasma potassium concentrations in patients that are receiving relatively low fluid rates. Potassium should not be added to fluids that are likely to be used for rapid intravenous infusion because of the risk of administration of a high dose quickly. Furthermore, inadequate mixing of intravenous fluids after addition of supplementary potassium can result in delivery of fluid with potassium concentrations an order of magnitude higher than expected.

Monitoring fluid therapy

Fluid requirements should be re-evaluated and adjusted regularly. In a patient receiving a bolus for hypovolaemia this may be every 15–30 minutes, whereas in a patient with chronic renal disease it may be on a daily basis. One of the most common mistakes with continued intravenous fluid therapy is failure to re-adjust fluid rates as the condition of the animal changes. There is a tendency to misconstrue the impressive autoregulatory abilities of the body (and more specifically the kidney) to infer that the choice of intravenous fluids is somewhat academic. Certainly, the normal kidney often compensates admirably for an inappropriate choice of fluid therapy. In animals with renal dysfunction or failure of the body's normal homeostatic mechanisms for water, electrolyte and acid–base balance, failure to select the appropriate fluid and monitor the effects may result in serious and potentially life-threatening complications. The most basic yet useful monitoring technique is the serial physical examination, which should include both assessment of perfusion and hydration parameters as well as evaluation for complications of fluid therapy (increased respiratory rate/effort, development of peripheral oedema). Other techniques discussed below may be used to augment the physical examination.

Bodyweight

Acute changes in bodyweight are largely due to changes in the fluid content of the body. When treating dehydrated patients, an increase in bodyweight is a positive sign that

euhydration is being restored. However, an increase in bodyweight in a non-dehydrated patient may be an early indicator that the patient is becoming fluid overloaded.

Serial bloodwork

It is recommended that PCV/TS and electrolytes are monitored frequently (at least daily) in patients on intravenous fluids. As discussed above, hypokalaemia is a common complication of chronic fluid therapy. In a patient with shock receiving aggressive fluid therapy, changes in PCV/TS can be used to guide the clinician as to when fluids such as colloids or blood products may be required. Lactate is a useful adjunct in the assessment of hypoperfusion, with a normal lactate level representing a suitable resuscitation endpoint in many patients. Central venous oxygen saturation (C_vO_2) greater than 70% is one of the resuscitation endpoints recommended in some human studies (Rivers *et al*., 2001); its use in veterinary patients is limited by the need to have a central line in place during the initial resuscitation period.

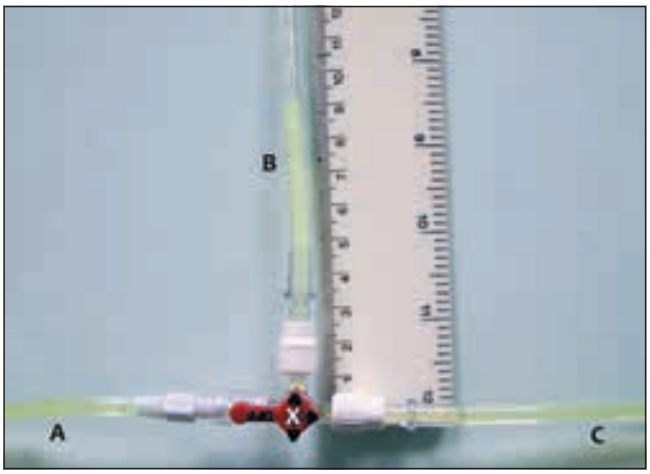
Arterial blood pressure

Arterial blood pressure is frequently measured in critically ill veterinary patients and reflects the interplay between cardiac output and systemic vascular resistance (see Chapter 3). Arterial hypotension is a late change in shock, as many of the homeostatic mechanisms act to maintain blood pressure. Fluid boluses are therefore often still warranted in patients that are normotensive on presentation, but which are showing signs of compensated shock. Arterial blood pressure monitoring may be used to monitor patients in hypotensive shock that are receiving fluid boluses to restore perfusion. A minimum systolic arterial pressure of 80–90 mmHg or mean arterial pressure of greater than 60 mmHg should be the initial goal. In normotensive patients, although there may be transient increases in arterial blood pressure in response to fluid boluses, arterial blood pressure does not continue to climb with further fluid loading and is thus less useful than central venous pressure for assessment of vascular filling.

Central venous pressure

The central venous pressure (CVP) is a measure of the hydrostatic pressure within the central venous compartment, and as such provides the most accurate assessment of vascular filling. It is typically measured via a catheter placed percutaneously into the jugular vein (see Chapter 2), which has its tip in the cranial vena cava. Catheters placed into the caudal vena cava via the saphenous or femoral veins may also be used but tend to give less predictable and less accurate readings. The CVP is measured by attachment of the central venous catheter to either an electronic pressure transducer or a water manometer. Electronic pressure transducers provide a continuous readout of CVP and allow assessment of the waveform; however, requires that practices have direct pressure monitoring equipment. A water manometer is used to provide intermittent readings of CVP and can be constructed from equipment available in most practices (three lengths of drip tubing, a ruler, a 60 ml syringe and a three-way stopcock; Figure 4.10).

Normal CVP is 0–5 cmH_2O. A low CVP implies inadequate vascular filling, whereas a high CVP implies intravascular volume overload, right-sided cardiac dysfunction, or increased intrathoracic pressure (e.g. pleural effusion). The change in CVP following a fluid bolus can be a useful guide to the necessity for further fluid loading, especially in patients in which volume overload is a concern, for example patients with possible anuric/oliguric renal failure. If the CVP is low, increases following a fluid bolus but then rapidly returns to pre-bolus levels, then more fluid therapy is warranted. In contrast, if it rises and remains high, this implies that the vascular volume is adequate and hypovolaemia is not the cause of the poor urine output.



4.10 A water manometer for measurement of central venous pressure (CVP). Tube A is attached to the central line in the patient and the patient is positioned in right lateral recumbency. For an accurate reading it is important that point X is at approximately the same height as the patient's right atrium. The three-way stopcock is closed to the patient. Tube B is filled with saline from a syringe attached to tube C, until the height of the water column is at least 20 cm. The three-way stopcock is then opened so that it allows communication between tubes A and B (i.e. off to tube C). The saline in tube B will run into the patient until the water column reaches a height that is in equilibrium with the patient's CVP. This height is read as the CVP in cmH_2O. Repeat measurements can be taken as often as necessary but for reliable interpretation the patient's position must be consistent. Note: for the purposes of this illustration, a coloured dye was added to the saline in this manometer.

Urine output

Urine output represents the balance between glomerular filtration rate (GFR) and tubular fluid reabsorption, and can be affected by a large number of different factors. It is thus impossible to define a 'normal' urine output but only to assess whether the output achieved is appropriate for the animal's clinical state. Assuming post-renal causes have been ruled out, critically ill patients may have a low urine output (<0.5 ml/kg/h) due to poor renal perfusion and low GFR (hypotension), anuric/oliguric renal failure, or high tubular reabsorption rate. The latter, which is associated with a high USG, implies that the animal's homeostatic mechanisms are actively conserving water and suggests normal renal function. In all of these instances, the goal should be to increase urine output into the 0.5–2.0 ml/kg/h range. In many cases this is achieved by providing the patient with adequate fluid therapy, although in the case of oliguric/anuric renal failure, pharmacological measures may be necessary to restart urine flow (see Chapter 8).

A falling urine output in a patient that had previously been considered to be volume replete can be an early indicator that the current fluid therapy plan is not supplying a sufficient volume of fluid. In most critical patients, this occurs because of changing and increased losses from the body, through the GI tract, wounds, or into third spaces. Patients may have an obligatory high urine output (>2 ml/kg/h and in some cases as high as 10–20 ml/kg/h) as a consequence of their underlying disease (e.g. polyuric

renal failure, post-obstructive diuresis). In this scenario, accurate monitoring of urine output helps guide the rate of intravenous fluid therapy that the patient requires. The goal in this situation should be to 'match ins with outs'.

Urine output is best measured by placement of an indwelling urinary catheter. Strict aseptic technique should be adhered to whenever handling the urinary catheter to reduce the risk of ascending urinary tract infection. Alternative methods include attempting to catch all the urine passed in ambulatory patients or weighing urine-soaked bedding in recumbent patients. Neither of these techniques is as accurate as catheterization.

Conclusion

Fluid therapy is an important part of the treatment of many critically ill veterinary patients. It should be remembered that fluids are a group of drugs just like any other, and have the potential to have adverse effects as well as positive ones. Numerous different fluids are available to veterinary practitioners, all of which can be used at a variety of different rates and doses. Successful fluid therapy comes from understanding why the patient requires fluid therapy and devising a fluid therapy plan for that individual based on both the goals of fluid treatment and an awareness of potential complications (Figure 4.11). Appropriate monitoring and a degree of flexibility with the plan as the patient's status changes are also important elements in achieving a successful outcome.

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Patient details
A 6-month-old, male entire Labrador Retriever, bodyweight 20 kg, presents with a history of 3 days of vomiting and diarrhoea that has been getting progressively worse. He is unvaccinated and a diagnosis of parvovirus is confirmed.

Physical examination
- Depressed
- HR = 170 bpm, cardiac auscultation is unremarkable
- Pulse quality weak/moderate
- Mucous membranes pale with a CRT of 2.5 seconds
- Respiratory rate and effort are within normal limits as is auscultation of the lungs
- When raised, the skin over the back of the neck falls back more slowly than normal

Minimum database
PCV = 39% (reference range: 37–55%), TS = 50 g/l (reference range: 57–70 g/l)
Glucose = 5.6 mmol/l (reference range: 3.5–5.5 mmol/l)
Azostix – BUN mildly elevated

Initial assessment
The patient requires fluids. He is showing evidence of moderate to severe hypoperfusion (tachycardia, abnormal pulse quality, abnormal mucous membranes) and moderate (~8%) dehydration. This is consistent with his history.

Initial plan
The hypoperfusion should be addressed first as it is potentially life-threatening. Plan to administer a fluid bolus of 50 ml/kg isotonic replacement crystalloid over 1 hour, with the aim of normalizing perfusion parameters. Fluid requirements = 50 x 20 = 1000 ml/h for 1 hour.

Assessment 1 hour later
Perfusion parameters have normalized (HR = 120 bpm, pulse quality improved, mucous membranes pink with 1.5 second CRT). Consider chronic fluid therapy plan. Need to calculate and sum for 24 hours:
- Replacement of hydration
- Maintenance
- Ongoing losses.

Replacement of hydration	
Fluid deficit	= % dehydration x bodyweight x 10 = 8 x 20 x 10 = 1600 ml
Maintenance	
Maintenance requirement	= 50 ml/kg/day = 50 x 20 = 1000 ml/day
Ongoing losses	
Ongoing losses	= diarrhoea + vomitus
Estimated diarrhoea volume/episode	= 100 ml x 5 episodes/day = 500 ml
Estimated vomitus volume/episode	= 50 ml x 5 episodes/day = 250 ml
Total ongoing losses	= 500 + 250 = 750 ml/day
Daily fluid requirement	= replacement + maintenance + ongoing losses = 1600 ml + 1000 ml + 750 ml = 3350 ml/day = 3350/24 ml/h = 140 ml/h

It should be recognized that this fluid rate is a 'best estimate' and may need to be increased or decreased depending on the patient's progression.

If perfusion parameters had not normalized at the end of the first fluid bolus, a second fluid bolus would have been required. The size of the second bolus and the type of fluid used should be chosen on the basis of the patient's physical examination at that time.

4.11 Example of a fluid therapy plan. BUN = blood urea nitrogen; CRT = capillary refill time; HR = heart rate; PCV = packed cell volume; TS = total solids.

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Chapter 5

Electrolyte and acid–base balance

Amanda Boag

The evaluation of electrolytes and acid–base status in critically ill patients is an important tool, both for helping to achieve a rapid diagnosis and for refining patient management. Furthermore, as we develop the veterinary evidence base using large clinical datasets, levels of these variables may be found to be prognostic (Holowaychuk and Monteith, 2011) or of use in modelling illness severity scoring systems for the critically ill patient (Hayes and Matthews, 2015). Electrolyte and acid–base parameters can change over very short time periods with disease progression or treatment, and the ability to measure these parameters in-house is essential. An increasing number of veterinary surgeons (veterinarians) have access to 'benchtop' machines such as i-Stat, epoc or VetStat blood gas analysers, allowing greater numbers of patients to benefit from the information they provide. For the emergency practitioner, a blood gas machine is more important for acute patient management than an in-house biochemistry machine. Hour-to-hour treatment decisions may be made on the basis of changes in electrolyte and acid–base status, whereas this is rarely the case with clinical biochemistry parameters.

This chapter reviews the relevant physiology and clinical significance of changes in the major electrolytes (sodium, potassium, chloride, calcium and magnesium) as well as providing an introduction to acid–base interpretation.

Sodium

Sodium is the most important osmotically active particle in the extracellular fluid (ECF) and, as such, is a vital determinant of ECF, and hence intravascular volume. The regulation of sodium concentration and water balance is intimately related, and most patients with clinically relevant hypo- or hypernatraemia have an underlying abnormality in the way the body handles water as opposed to an increased or decreased amount of sodium. The nephrons of the kidney are the prime site for sodium and water homeostasis, where the endocrine mechanisms for volume regulation (i.e. sodium content) and osmoregulation (i.e. water content) are integrated. The body regulates ECF volume by altering the amount of sodium excreted; volume regulation involves detection of intravascular volume changes at a number of anatomical sites (carotid sinus, aortic arch, glomerular afferent arterioles, cardiac atria), with alterations in the activation of the renin–angiotensin–aldosterone system (RAAS), the sympathetic nervous system (SNS) and atrial natriuretic peptide (ANP) being the principal effector mechanisms. The complex actions of these hormones lead to either increased (RAAS, SNS) or decreased (ANP) sodium retention by the kidneys. Osmoregulation involves detection of changes in osmolality by the hypothalamus with control effected by antidiuretic hormone (ADH; vasopressin). An increase in ADH leads to increased body water by stimulating thirst and increasing water reabsorption in the distal part of the nephron. At times the regulation of ECF volume and osmolality may conflict (for example the hypovolaemic patient with hypernatraemia) and in this scenario, maintenance of an effective circulating fluid volume is prioritized over normalizing osmolality. The reader is referred to the References and further reading section for sources with more detail on the physiology of this important topic.

Ultimately, the measured serum sodium concentration reflects the balance between the amount of sodium relative to the amount of water within the ECF compartment, and is not a direct indicator of total body sodium. Patients with hypernatraemia (or hyponatraemia) may therefore have normal, increased or decreased total body sodium in different disease situations. For example, a patient with significant loss of hypotonic fluid (e.g. due to osmotic diarrhoea) may have *decreased* total body sodium, but actually be *hyper*natraemic if the loss of water exceeds the loss of sodium. These patients are likely to be hypernatraemic and hypovolaemic. Conversely, a patient with hypernatraemia secondary to excessive intake of salt (impermeant solute gain), which also has had access to water, may be hypernatraemic and hypervolaemic. When evaluating patients with sodium abnormalities it is vitally important to make an assessment of intravascular volume status on the basis of physical examination and history (see Chapter 4). Recognition of the patient's volume status allows refinement of the differential diagnosis list and has important implications for treatment. As the sodium ion is monovalent, 1 mmol/l is equivalent to 1 mEq/l.

Disorders of sodium

Causes

The differential diagnoses for sodium abnormalities, categorized according to the patient's intravascular volume status, are shown in Figure 5.1. Several of the causes (e.g. vomiting and diarrhoea) may cause either hyper- or hyponatraemia depending on the exact nature of the losses (i.e. whether they contain more sodium than water or *vice versa*) and the ability of the animal to drink and regain free

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Hypernatraemia

- Hypervolaemia (impermeant solute gain)
  - Salt poisoning
  - Iatrogenic (hypertonic saline administration)
- Normovolaemia (pure water deficit)[a]
  - *Hyperthermia*
  - Diabetes insipidus (central/nephrogenic)
  - Inadequate access to water
  - Primary hypodipsia
- Hypovolaemia (loss of water in excess of sodium)
  - *Renal failure (acute or chronic)*
  - *Vomiting and diarrhoea*
  - Burn injuries
  - Drug-induced (furosemide, mannitol)

Hyponatraemia

- Hypervolaemia (impaired water excretion)
  - *Congestive heart failure*
  - *Severe hepatic disease*
  - *Renal disease (nephrotic syndrome)*
- Normovolaemia
  - Syndrome of inappropriate ADH secretion (SIADH)
  - *Hypotonic fluid administration*
  - Psychogenic polydipsia
- Hypovolaemia (loss of sodium in excess of water)
  - *Hypoadrenocorticism*
  - *Vomiting and diarrhoea*
  - *Drug-induced (diuretics)*
- Third-space loss

5.1 Differential diagnosis of serum sodium abnormalities. Diagnoses in *italics* are those encountered most frequently in clinical practice. [a]Although the conditions listed here initially lead to normovolaemic hypernatraemia, in clinical practice, by the time patients with pure water deficit present to a veterinary surgeon, they are often exhibiting signs of hypovolaemia. ADH = antidiuretic hormone.

water. The presence and influence of other osmotically active particles in the plasma should also be considered when interpreting serum sodium values. This is clinically most relevant when evaluating diabetic patients. In these patients, the elevated serum glucose acts as an osmotically active particle and draws water into the vasculature, leading to dilution of the serum sodium. It is expected that for every 1 mmol/l increase in glucose, the serum sodium will be reduced by approximately 0.3–0.4 mmol/l.

Finally, when assessing patients with hyponatraemia, the possibility of pseudohyponatraemia should be considered. This is an artefact that occurs when serum sodium is measured by flame photometry (used by most commercial laboratories) in patients with concurrent hyperlipidaemia or hyperproteinaemia. In this situation the true serum sodium is likely to be within normal limits. Pseudohyponatraemia has no negative clinical consequences but it is important that it is recognized so that the low serum sodium is not over interpreted.

Clinical signs

Mild abnormalities in serum sodium are common and rarely cause clinical signs. If sodium abnormalities are moderate to severe (<130 mmol/l or >170 mmol/l) and especially if they develop rapidly, clinical signs may ensue. The clinical signs are principally neurological. With hypernatraemia, the increased tonicity of the ECF leads to movement of water out of brain cells, causing cerebral dehydration and development of neurological signs. With hyponatraemia, the decreased ECF tonicity promotes movement of water into the brain, with development of cerebral oedema. The rate of change in sodium is an important determinant of the severity of the clinical signs. If the sodium abnormality develops slowly (i.e. over a period of days to weeks), the brain is able to compensate and clinical signs may not be seen. When hypernatraemia progresses gradually, the brain generates inert intracellular substances known as idiogenic osmoles that counteract the increased ECF tonicity and prevent cerebral fluid loss. With gradual onset of hyponatraemia, the brain is able to adjust by losing osmotically active particles. This has important implications for treatment, in that rapid correction of chronic sodium abnormalities may precipitate clinical signs that are more severe than those induced by the sodium abnormality itself.

Treatment

The principles of treatment for both hyper- and hyponatraemia are similar, and generally involve manipulation of the patient's intravenous fluid therapy. For the majority of patients with serum sodium abnormalities, the serum sodium concentration does not need specific treatment but will correct itself as the underlying disease is treated. Patients with clinical signs may, however, require treatment aimed specifically at the sodium abnormality. It is also vital to ensure that treatment for the underlying disease does not lead to rapid changes in sodium and development of iatrogenic clinical signs.

When the serum sodium abnormality has been gradual in onset, the serum sodium should be corrected slowly, with a maximum change of 0.5 mmol/l sodium per hour in either direction.

If hypovolaemia is also present, initial treatment should be directed at restoration of the patient's intravascular volume with the use of fluid boluses (see Chapter 4). To avoid rapid changes in the patient's serum sodium, the fluid chosen for boluses should have a sodium concentration close to the animal's serum sodium. For the majority of hypernatraemic patients 0.9% NaCl (sodium concentration 154 mmol/l) is suitable, and for hyponatraemic patients, Hartmann's solution (sodium concentration 131 mmol/l) or lactated Ringer's solution (sodium concentration 134 mmol/l) are the fluids of choice. Once the animal's intravascular volume status has been restored, the serum sodium concentration can be returned to normal over a period of 24–48 hours. Where possible, hypernatraemic patients should be encouraged to drink and regain their free water by that route. If the patient is vomiting or unable to drink (e.g. with neurological disease), free water must be administered using hypotonic fluids (0.45% NaCl, 5% dextrose in water). The patient's approximate free water deficit can be calculated using the following equation:

$$\text{Free water deficit (l)} = 0.6 \times \text{current weight (kg)} \times \left(\frac{\text{serum sodium concentration (patient)}}{\text{serum sodium concentration (normal)}} - 1 \right)$$

This volume of free water can then be administered gradually over the number of hours calculated to restore normal serum sodium whilst remaining within the recommended maximum rate of change of 0.5 mmol/l/h. An example calculation is given in Figure 5.2. Frequent monitoring of sodium is recommended (up to every 2–4 hours) to ensure that the sodium is not changing too rapidly. The fluid therapy plan may need to be adjusted frequently during this time period.

The majority of normo- or hypervolaemic, hyponatraemic patients are asymptomatic for their hyponatraemia. Treatment commonly involves medical therapy directed at the underlying cause (see Figure 5.1), although in many

A 6-month-old Staffordshire Bull Terrier with hypodipsia since birth presents with serum sodium of 190 mmol/l. Current bodyweight is 15 kg.

Free water deficit = $0.6 \times 15 \times \left(\frac{190}{145} - 1\right)$

Free water deficit = 2.8 l

This should be administered to return the sodium to the normal range (145–155 mmol/l) at a rate no greater than 0.5 mmol/l/h. As the objective is for serum sodium to drop 35 mmol/l (from 190 mmol/l to 155 mmol/l), this should occur over 70 hours.

If 5% dextrose in saline is used, this is equivalent to 100% free water, thus the rate of fluid administration would be 2800/70 = 40 ml/h.

If 0.45% NaCl is used, this represents 50% free water, thus the rate of fluid administration would be (2800/70) x 2 = 80 ml/h.

Any ongoing electrolyte losses should also be taken into consideration, with concurrent administration of isotonic fluids if necessary.

5.2 Example of free water deficit calculation.

patients with chronic diseases such as congestive heart failure, the hyponatraemia may remain and its correction is not the prime goal of treatment. If fluid therapy is required in these patients, careful consideration should be given to the underlying disease process and the reason for administration of fluids. In many instances a fluid with a sodium concentration slightly greater than the patient's serum sodium is appropriate. In patients with symptomatic hyponatraemia (typically Na^+ <120 mmol/l), more targeted treatment may be needed, with use of diuretics to promote free water loss or administration of small quantities of hypertonic saline. The rate at which the serum sodium will change is very difficult to predict and too rapid correction may lead to irreversible neurological signs secondary to cerebral myelinolysis. As with correction of hypernatraemia, frequent monitoring of serum sodium is required with adjustment of the fluid therapy plan as necessary.

Potassium

Potassium is the most abundant intracellular cation. Approximately 95–98% of total body potassium is found within the cells, and intracellular potassium concentration is approximately 140 mmol/l. Serum potassium is maintained within a much lower and very narrow range (approximately 3.5–5.5 mmol/l); this difference between intracellular and extracellular concentrations is vitally important for determining the resting membrane potential of excitable tissues (including cardiac conduction tissue). Serum concentrations do not reflect whole-body potassium levels. Translocation between the extracellular and intracellular compartments can be a cause of potassium abnormalities, or may be utilized during treatment. Potassium intake is principally via the gastrointestinal tract and typically exceeds daily potassium requirements. The excess potassium is excreted mainly via the urinary system, with aldosterone being the principal hormone affecting potassium excretion in the distal tubule. As the potassium ion is monovalent, 1 mmol/l is equivalent to 1 mEq/l.

Hyperkalaemia

Causes

Causes of hyperkalaemia may be divided into those that occur secondary to reduced renal excretion of potassium, and those that involve translocation of potassium from the intracellular to the extracellular compartment. Rarely, increased intake of potassium may lead to hyperkalaemia. The differential diagnoses are shown in Figure 5.3. Artefactual hyperkalaemia can also be caused by improper sample handling, especially the use of blood anticoagulated with ethylenediaminetetraacetic acid (EDTA) for electrolyte measurement, thrombocytosis or haemolysis in some breeds (e.g. Akitas) whose red cells have a high potassium concentration.

Decreased urinary excretion

- *Uroabdomen*
- *Urethral obstruction*
- *Hypoadrenocorticism*
- Anuric/oliguric renal failure
- Effusive disorders (pleural, peritoneal, pericardial)
- Gastrointestinal disease (e.g. trichuriasis, salmonellosis, perforated duodenum)
- Drug-induced:
  - Angiotensin-converting enzyme inhibitors
  - Potassium-sparing diuretics

Translocation from intracellular to extracellular compartment

- Massive cell death:
  - Reperfusion injury following thromboembolism
  - Severe trauma
  - Tumour lysis syndrome
  - Heatstroke
- Acute mineral acidosis
- Insulin deficiency
- Drug-induced:
  - Beta-blockers

Increased intake

- Iatrogenic

5.3 Differential diagnosis of hyperkalaemia. Diagnoses in *italics* are those encountered most frequently in clinical practice.

Clinical signs

The most life-threatening consequence of hyperkalaemia is its effect on myocardial conduction. Clinically, this is detected by an inappropriate bradycardia and characteristic electrocardiogram (ECG) changes. As serum potassium increases, initially there is a prolonged PR interval, decreased R wave amplitude and increased T wave amplitude. This progresses to atrial standstill (absent P wave) with widened QRS complexes and bradycardia (see Chapter 6). A 'sine wave' trace may be seen shortly before asystole. A serum potassium level of >7.5 mmol/l should be considered of great concern, although precise correlation between the magnitude of the hyperkalaemia and the ECG changes does not exist, as other factors (e.g. acid–base status, ionized calcium levels) also affect myocardial conduction. Treatment should therefore be based on the severity of the ECG changes and their clinical effects on the patient, rather than simply on the measured serum potassium level.

Treatment

Emergency treatment of hyperkalaemia is required whenever the patient has high serum potassium and is showing consistent clinical or ECG changes. If serum potassium cannot be measured in-house but the index of suspicion for hyperkalaemia is high (e.g. bradycardia in a patient with urethral obstruction), treatment should still be considered. Specific treatment for hyperkalaemia includes:

- Intravenous calcium gluconate at a dose of 0.5–1.5 ml/kg of a 10% solution given intravenously over 5–10 minutes. This acts rapidly to counteract the effects of the high potassium on myocardial

conduction. Its effects last approximately 20 minutes and the dose can be repeated. It does not lower serum potassium but is the first-choice therapy in severely affected animals due to its rapidity of action

- Regular (soluble) insulin at a dose of 0.25–0.5 IU/kg administered intravenously with 2 g dextrose per unit of insulin and followed by the addition of 2.5% dextrose to the intravenous fluids. Insulin acts to lower serum potassium by promoting potassium uptake into cells along with glucose. It takes about 20 minutes to have an effect. It is essential that intravenous fluids are supplemented with glucose for 12–24 hours following this treatment to prevent the development of hypoglycaemia
- Sodium bicarbonate at a dose of 1–2 mmol/kg administered intravenously over 15 minutes. This acts to drive potassium intracellularly by changing plasma pH. It is rarely necessary and should only be used if the acid–base status can be monitored
- Terbutaline at a dose of 0.01 mg/kg intravenously slowly. This stimulates the Na^+/K^+ ATPase to translocate potassium intracellularly.

Most patients with hyperkalaemia also have significant abnormalities of fluid balance and are frequently hypovolaemic. As such, almost all these patients also require intravenous fluid therapy with a replacement crystalloid fluid. The fluid should be chosen after consideration of all the patient's electrolyte abnormalities. Although Hartmann's solution/lactated Ringer's solution contains small amounts of potassium, this small dose is unlikely to have a clinical impact on the patient in comparison with the dilution produced by fluid administration. In a study evaluating electrolyte changes in cats with urethral obstruction receiving either 0.9% NaCl or lactated Ringer's solution, there was no significant difference between fluid groups in the speed of correction of the potassium, but the acid–base status was corrected more rapidly in the patients receiving lactated Ringer's solution (Cole and Drobatz, 2003).

Alongside emergency treatment of the hyperkalaemia, it is important to identify and treat the underlying cause. This may include placing a urethral catheter (urethral obstruction; see Chapter 8), surgery (uroabdomen; see Chapter 12) or medical therapy (acute renal failure, hypoadrenocorticism; see Chapters 8 and 16, respectively).

Hypokalaemia

Causes

Hypokalaemia is a common finding in critically ill patients, especially those which are inappetent and on long-term fluid therapy. Causes include decreased intake, increased loss through either the kidneys or gastrointestinal tract, or translocation from the extracellular to the intracellular compartment. The differential diagnoses are summarized in Figure 5.4.

Clinical signs

The physiological consequences of hypokalaemia are generally less imminently life-threatening than those associated with hyperkalaemia. Signs are typically non-specific and consist of weakness, lethargy, ileus and anorexia. In cats, ventroflexion of the neck may be seen. As these signs may contribute to patient morbidity, correction of even mild hypokalaemia is recommended. Severe hypokalaemia (serum potassium <2.8 mmol/l) can lead to respiratory muscle weakness and hypoventilation, with the potential to progress to respiratory paralysis and death. Potassium depletion also produces abnormalities within the kidney (hypokalaemic nephropathy), a feature of which is impaired responsiveness to ADH. This leads to polyuria and further renal potassium losses.

Increased loss

- Gastrointestinal tract
  - *Vomiting*
  - *Diarrhoea*
- Urinary tract
  - *Chronic renal failure (particularly cats)*
  - *Postobstructive diuresis*
  - Drug-induced:
    - *Diuretics (loop, thiazide)*
  - Penicillins
  - Mineralocorticoid excess
  - Renal tubular acidosis

Translocation from extracellular to intracellular compartment

- Insulin/glucose-containing fluids
- Alkalaemia
- Catecholamine release
- Refeeding syndrome

Decreased intake

- *Inappetence/anorexia*
- *Long-term administration of intravenous fluid with low potassium concentration*

5.4 Differential diagnosis of hypokalaemia. Diagnoses in *italics* are those encountered most frequently in clinical practice.

Treatment

Hypokalaemia is treated with potassium supplementation via the oral or intravenous route. In critically ill patients the intravenous route is used most frequently, by adding potassium chloride to the intravenous fluids. In an anorexic patient receiving an isotonic replacement fluid (e.g. Hartmann's, 0.9% NaCl) at maintenance rates, addition of 14–20 mmol K^+/l is usually sufficient to maintain serum potassium levels. If the patient has pre-existing hypokalaemia higher rates of supplementation may be needed (Figure 5.5). All fluids to which potassium chloride has been added must be well mixed and clearly labelled. These fluids should never be administered as a bolus due to the potential effects of rapid intravenous potassium infusion on cardiac conduction. Potassium should not generally be infused at a rate greater than 0.5 mmol/kg/h, although in patients with profound symptomatic hypokalaemia rates of 1–1.5 mmol/kg/h may be used. It is recommended that if rates approaching 0.5 mmol/kg/h are used, the patient is monitored continuously with an ECG, and this is mandatory if rates greater than 0.5 mmol/kg/h are used. If the patient is eating voluntarily or has a feeding tube in place, enteral potassium supplementation is safe and effective. The dose of enteral potassium required is difficult to predict and monitoring of serum potassium is advised; a suggested initial dose is 0.5–1.0 mmol/kg orally twice daily.

Serum potassium (mmol/l)	KCl (mmol) to add to 1 l fluids	Maximum recommended infusion rate for supplemented fluids (ml/kg/h)
3.5–5.0	20	25
3.0–3.5	30	18
2.5–3.0	40	12
2.0–2.5	60	8
<2.0	80	6

5.5 Guidelines for supplementation of intravenous fluids with potassium chloride (KCl) for the treatment of hypokalaemia.

Chloride

Chloride is the major extracellular anion and serum chloride levels generally change in a similar way to those of serum sodium. Treatment of the sodium abnormality generally leads to concurrent resolution of the chloride abnormality. Chloride has an important role in acid–base balance due to its interactions with renal sodium and bicarbonate reabsorption.

Hyperchloraemia

Hyperchloraemia rarely requires specific treatment and is commonly accompanied by hypernatraemia, which is of greater clinical significance. The presence of hyperchloraemia may aid with interpretation of acid–base abnormalities (see Metabolic acid–base disturbances). Artefactual hyperchloraemia may be seen in patients receiving potassium bromide therapy for management of seizures. These patients generally have normal serum sodium.

Hypochloraemia

Hypochloraemia is of clinical relevance principally because of its effects on systemic acid–base balance. Hypochloraemic patients are prone to developing a metabolic alkalosis, especially if they have concurrent hypovolaemia with avid renal retention of sodium. As sodium is reabsorbed, the nephron must also reabsorb or regenerate anions in order to maintain electroneutrality. The anion reabsorbed is principally chloride, but in situations of chloride depletion, bicarbonate (HCO_3^-) is regenerated instead, thus predisposing the patient to the development of alkalaemia. Clinically, this is seen in patients with severe vomiting that develop a significant hypochloraemic metabolic alkalosis. Use of 0.9% NaCl as the resuscitative fluid of choice in these patients will aid the restoration of acid–base balance, as the higher chloride concentration allows the kidneys to excrete the bicarbonate whilst continuing active sodium retention.

Calcium

Calcium has many important extracellular and intracellular functions, as well as being a major component of the skeleton. Extracellular calcium consists of three fractions:

- Ionized calcium (iCa^{2+}): this forms about 55% of total calcium and is the physiologically active fraction. As calcium is divalent, 1 mmol/l is equivalent to 2 mEq/l
- Complexed calcium: this forms about 10% of total calcium and consists of calcium complexed to anions such as citrate, lactate and bicarbonate
- Protein-bound calcium: this forms about 35% of total calcium.

The total calcium value reported by most in-house biochemistry machines and external laboratories represents all three fractions, whereas blood gas machines more commonly measure the ionized calcium fraction. It is important to know which component has been measured when interpreting calcium abnormalities. Ideally, the ionized calcium should be measured, as this is the biologically active component. Although equations have been suggested to predict the ionized calcium concentration from the total calcium value and serum albumin, they are not accurate and are not recommended (Schenk and Chew, 2005; Schenk and Chew, 2010).

Calcium intake is principally via the gastrointestinal tract, with excretion via the kidneys. Calcium stored in bone can also be mobilized in response to hypocalcaemia. Three hormone systems are involved principally with calcium homeostasis:

- Parathyroid hormone (PTH): a peptide hormone secreted by the parathyroid gland, PTH leads to increased plasma iCa^{2+} by reducing renal calcium excretion, increasing bone resorption and increasing calcium absorption from the gastrointestinal tract (via calcitriol). Parathyroid hormone-related peptide (PTHrP) is a PTH-like substance that is secreted by some tumours and is often responsible for the humoral hypercalcaemia of malignancy
- Calcitonin: a peptide hormone secreted by the C cells of the thyroid gland, leading to decreased iCa^{2+} by inhibiting bone resorption
- Calcitriol (1,25-dihydroxycholecalciferol): a steroid hormone manufactured in the kidneys in response to increased PTH, calcitriol acts to increase iCa^{2+} by increasing gastrointestinal absorption and bone resorption.

Hypercalcaemia

Causes

The causes of hypercalcaemia may be divided into those in which the ionized calcium is elevated (Figure 5.6) and those in which the total calcium is elevated but the ionized calcium is normal. The latter situation may occur due to increases in the protein-bound fraction (increased albumin with dehydration) or increases in the complexed fraction (e.g. in chronic renal failure because there is an increase in many of the anions with which calcium forms complexes). Young growing animals have a mild physiological ionized hypercalcaemia. Emergency treatment for hypercalcaemia is warranted only if the ionized calcium is increased.

- Neoplasia:
  - *Lymphoma*
  - *Anal sac adenocarcinoma*
  - Multiple myeloma
  - Carcinoma (including mammary, prostatic, thyroid)
  - Thymoma
- *Primary hyperparathyroidism*
- Acute renal failure
- *Hypoadrenocorticism*
- Granulomatous disease:
  - *Angiostrongylus vasorum* infection
  - Fungal disease
  - Sterile dermatitis/panniculitis
- Vitamin D toxicosis:
  - Some rat poisons
  - Psoriasis cream
- Non-neoplastic disorders of bone
- *Idiopathic* (cats)

5.6 Differential diagnosis of ionized hypercalcaemia. Diagnoses in *italics* are those encountered most frequently in clinical practice.

Clinical signs

Clinical signs of hypercalcaemia are often vague and non-specific. Typically, patients are inappetent (or anorexic), lethargic and polyuric/polydipsic. Vomiting, constipation, cardiac dysrhythmias and muscle twitching are less common clinical signs. The increased calcium affects the

kidney's ability to respond to ADH (a form of nephrogenic diabetes insipidus), therefore patients may have a pre-renal azotaemia with relatively dilute urine. If the hypercalcaemia is prolonged, severe and/or associated with a high phosphate level, soft tissue mineralization of several organs may occur. Renal mineralization leads to the development of renal failure, which is the most serious complication of untreated hypercalcaemia.

Treatment

Definitive treatment of hypercalcaemia usually involves identification and treatment of the underlying cause. The diagnostic work-up may, however, take some time and therapy specifically to manage the calcium may be necessary during this period. Treatment should be instituted if the animal has a high iCa^{2+} level and/or is showing clinical signs related to hypercalcaemia. Soft tissue mineralization is more likely to occur if the total calcium (mmol/l) x phosphorus (mmol/l) product is >5 (>60 if these electrolytes are measured in mg/dl), and aggressive treatment should be implemented in these animals to reduce the risk of renal failure. Treatment options include:

- Fluid diuresis with 0.9% NaCl at 4–6 ml/kg/h. The high renal sodium load promotes calciuresis
- Furosemide at 1–2 mg/kg every 6–12 hours to promote renal calcium excretion. This diuretic should only be used after dehydration has been corrected with fluid therapy
- Salmon calcitonin at a dose of 4–7 IU/kg s.c. q6–8h. As salmon calcitonin is a foreign antigen, there is a theoretical risk of anaphylaxis, especially with multiple doses
- Bisphosphonates, which act to reduce bone resorption. The dose depends on the preparation used and is not well defined in small animal species. The author has used clodronate at 10 mg/kg diluted in 0.9% NaCl as a slow infusion over 4–6 hours, with success in reducing iCa^{2+} and minimal apparent side effects
- Peritoneal dialysis or haemodialysis for life-threatening hypercalcaemia
- Glucocorticoids at anti-inflammatory doses. Glucocorticoids act by several mechanisms to reduce serum calcium; however, they may also interfere with tests necessary to diagnose the underlying cause, and therefore compromise future treatment options. It is recommended that they are only used once the diagnostic evaluation has been completed.

Saline diuresis and furosemide are successful in controlling mild to moderate hypercalcaemia in the short term in the majority of patients. More severe hypercalcaemia often associated with toxicity is more likely to require aggressive measures. Long-term treatment relies on identification of the underlying cause with appropriate specific treatment. Diagnostic tests to be considered include a thorough physical examination (including rectal examination), toxicological history, thoracic and abdominal imaging, aspiration of any masses or enlarged lymph nodes, PTH and PTHrP levels, bone marrow aspiration and tests for infectious diseases as suggested by geographical location. Specific treatment may involve surgery (e.g. to remove a parathyroid tumour), chemotherapy or treatment of infectious disease. The prognosis depends on the underlying disease. Patients that have already developed renal failure secondary to hypercalcaemia have a poorer prognosis. The hypercalcaemia seen with vitamin D toxicosis tends to carry a poor prognosis as it is typically of high magnitude, of long duration and is associated with high serum phosphorus.

Hypocalcaemia

Causes

As with hypercalcaemia, it is important to assess whether hypocalcaemia represents an ionized hypocalcaemia (which may lead to clinical signs) or a total hypocalcaemia related to a low serum albumin concentration. Ionized hypocalcaemia is a relatively common finding in critically ill patients and may be prognostic (Luschini *et al*., 2010; Holowaychuk and Monteith, 2011; Dias and Carreira, 2015). Causes of ionized hypocalcaemia are shown in Figure 5.7. Artefactual hypocalcaemia can be caused by improper sample handling, especially testing using blood anticoagulated with EDTA.

- Hypoparathyroidism:
  - Primary
  - *Iatrogenic (post-thyroidectomy)*
  - Nutritional secondary hypoparathyroidism
- *Chronic renal failure*
- *Eclampsia (puerperal tetany)*
- Ethylene glycol toxicity
- *Acute pancreatitis*
- Sepsis
- Severe intestinal malabsorption
- Iatrogenic:
  - Phosphate enema
  - Rapid or massive administration of blood products (citrate toxicity)
  - Rapid administration of phosphate-containing fluids
  - Excessive bisphosphonate administration
- Hypomagnesaemia
- Hypovitaminosis D

5.7 Differential diagnosis of ionized hypocalcaemia. Diagnoses in *italics* are those encountered most frequently in clinical practice.

Clinical signs

Low serum iCa^{2+} leads to increased excitability of neuromuscular tissue. Common clinical signs include muscle tremors, facial rubbing, behavioural changes, stiff gait, panting and hyperthermia. If severe, the patient may exhibit tetany, ECG changes (prolonged QT interval) and hypotension. Ultimately, severe hypocalcaemia can cause respiratory arrest and death.

Treatment

In the patient presenting with signs of tetany, urgent treatment with intravenous calcium is warranted. Calcium gluconate (10%) is given slowly intravenously to effect. The typical dose is 0.5–1.5 ml/kg administered over 10–20 minutes. Patients should be monitored by ECG during administration, if possible. The infusion should be discontinued if the patient becomes bradycardic or develops a short QT interval. If an ECG is not available, pulse quality and heart rate should be monitored closely. Following resolution of the immediate crisis, supplementation with calcium gluconate can be continued if necessary as an intravenous infusion. The dose required is very variable dependent on the cause of the hypocalcaemia, ranging from 1–15 mg elemental calcium/kg/h. Subcutaneous administration is not recommended. Calcium chloride is an alternative formulation, but it is caustic and should only be administered with extreme care intravenously and never subcutaneously. Calcium gluconate contains 9.3 mg elemental calcium per ml, whereas calcium chloride contains 27.2 mg elemental calcium per ml.

In critically ill patients with stable asymptomatic hypocalcaemia, treatment may not be necessary and the

hypocalcaemia may resolve with the underlying disease; although hypocalcaemia has been associated with a poorer prognosis, there is no evidence that treatment would impact this. However, if subtle clinical signs exist or the ionized calcium is progressively falling, treatment with addition of a constant rate infusion (CRI) of calcium to the fluid regime should be considered. If the underlying cause of hypocalcaemia cannot be resolved, chronic management with oral vitamin D or calcium supplementation may be required.

Magnesium

Magnesium is measured less frequently than the other electrolytes; however, a small number of clinical studies have shown magnesium abnormalities to be present in a high proportion of critically ill dogs and cats (Martin *et al*., 1994; Toll *et al*., 2002). In human medicine hypomagnesaemia is one of the most commonly seen electrolyte disturbances in critically ill patients. Magnesium has a role in many intracellular processes, including the synthesis and degradation of DNA, oxidative phosphorylation and the production of second messengers (e.g. cAMP). It is also important for normal cardiac and neuromuscular function and is involved with potassium regulation at the level of the kidney. Clinical signs associated with hypomagnesaemia include refractory hypokalaemia, cardiac conduction disturbances and increased neuromuscular excitability. The incidence and clinical importance of these signs has yet to be determined in small animal patients; however, normalization of serum magnesium levels is recommended if serum magnesium is low and one or more compatible clinical signs are present (Humphrey *et al*., 2015). Magnesium sulphate or magnesium chloride should be administered as a slow intravenous infusion at a dose of 0.375–0.5 mmol/kg/day. As the magnesium ion is divalent, 1 mmol/l is equivalent to 2 mEq/l.

Magnesium is excreted through the kidneys, therefore hypermagnesaemia is most commonly seen in patients with reduced glomerular filtration rate, and generally does not require specific treatment. Hypermagnesaemia associated with iatrogenic overdose has been reported (Jackson and Drobatz, 2004).

Acid–base abnormalities

Maintenance of pH within a strict range is essential for normal cellular function, as many intracellular enzymatic processes are pH-dependent. On a daily basis, the body produces large amounts of both carbon dioxide (also called volatile acid) as a by-product of the metabolism of carbohydrate and fat, and hydrogen ions (H^+) as a by-product of the metabolism of proteins and phospholipids. The carbon dioxide is excreted through the lungs and the hydrogen ions are excreted through the kidneys. Carbon dioxide is an acid in solution due to its ability to combine with water, in the presence of carbonic anhydrase, to produce carbonic acid:

$$CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$$

To facilitate handling of the daily acid load, the body has several buffer systems, the most important of which is bicarbonate. Other buffers include haemoglobin and plasma proteins. Bicarbonate is constantly regenerated and added back to the circulation by the kidneys. Many pathological processes affect the body's ability to maintain a normal pH.

Measurement of acid–base status in emergency and critically ill patients has many uses including:

- Early identification of some diagnoses, e.g. ketoacidosis in a vomiting patient with an unexplained metabolic acidosis
- Production and refinement of complete problem and differential diagnosis lists
- Monitoring response to therapy, e.g. resolution of lactic acidosis in a patient with hypovolaemic shock following appropriate fluid therapy
- Prompting specific treatment when the acid–base abnormality is severe enough to be life-threatening, e.g. starting (or increasing) artificial ventilation of patients with severe hypercarbia (P_aCO_2 >60 mmHg)
- Optimizing therapy for an individual patient, e.g. choice of 0.9% NaCl as opposed to a fluid with lower chloride concentration for use in a patient with a hypochloraemic metabolic alkalosis.

Interpretation of acid–base abnormalities is often regarded as challenging and there is ongoing debate about the best way to interpret results in patients with complex acid–base disturbances. However, for the majority of patients the traditional approach to blood gas interpretation, utilizing pH, partial pressure of CO_2 (PCO_2) and bicarbonate (or base excess), provides sufficient information for effective clinical use.

Definitions

- pH: a familiar measure of acidity/alkalinity calculated as the negative log of the hydrogen ion concentration.
- Acidaemia: blood pH <7.35.
- Alkalaemia: blood pH >7.45.
- Acidosis: a process that tends to lead to acidaemia. It may not result in acidaemia if there is adequate compensation, or if there is a concurrent process tending to lead to alkalaemia.
- Alkalosis: a process that tends to lead to alkalaemia. It may not result in alkalaemia if there is adequate compensation or if there is a concurrent process tending to lead to acidaemia.
- Respiratory acidosis/alkalosis: where the process leading to the acid–base disturbance involves abnormalities of the concentration (partial pressure) of the volatile acid carbon dioxide.
- Metabolic acidosis/alkalosis: where the process leading to the acid–base disturbance involves abnormalities of acid/alkali other than carbon dioxide.
- Base excess (BE): a calculated value that is a reflection of the non-respiratory portion of acid–base balance. It takes into account all of the body's buffer systems and is closely (but not linearly) related to bicarbonate. A negative value indicates the presence of a metabolic acidosis whereas a positive value indicates the presence of a metabolic alkalosis.
- Compensation: mechanisms by which the body attempts to maintain a normal pH despite disturbances in the acid–base status. With a primary metabolic acid–base disturbance, compensation is via the respiratory system, with alterations in ventilation and the excretion of carbon dioxide. This respiratory compensation occurs very rapidly over minutes to

hours. With a primary respiratory acid–base disturbance, there is compensation on the metabolic side, by alterations in the excretion of acid load through the kidneys. This metabolic compensation occurs gradually over days. Compensation can be very effective and may return the pH to within the normal range. Importantly, overcompensation never occurs.

- Primary acid–base disturbance: the initial (usually the most severe) disturbance in acid–base status. Primary acid–base disturbances may be accompanied by compensatory changes. Examples might include a cat with urethral obstruction and a primary metabolic acidosis secondary to reduced renal excretion of the daily acid load. This cat may also be tachypnoeic, as acidosis leads to an increase in minute ventilation, producing a compensatory respiratory alkalosis.
- Mixed acid–base disturbances: more than one primary acid–base disturbance occurring concurrently. Examples might include:
  - A patient with pneumonia and septic shock. This patient may have a respiratory alkalosis, as it increases ventilation to try to maximize oxygenation, and a metabolic (lactic) acidosis secondary to the septic shock and inadequate tissue perfusion
  - A dog with pyloric obstruction and vomiting of gastric contents, which is also in hypovolaemic shock. This patient may have a metabolic alkalosis secondary to vomiting of hydrochloric acid-rich stomach contents, and a metabolic (lactic) acidosis secondary to hypovolaemic shock and reduced tissue perfusion. This patient may have a normal pH at presentation because the two primary processes balance each other out, but could become significantly alkalaemic as the shock is treated with intravenous fluids.

Approximate reference values for acid–base parameters in arterial blood are shown in Figure 5.8. Venous blood differs slightly because carbon dioxide produced by tissue metabolism has been added as it passes through the capillary bed, therefore venous blood tends to have a slightly lower pH and higher PCO_2. In all situations other than complete circulatory collapse venous blood is considered to be adequate for assessment of acid–base status (Ilkiw *et al*., 1991).

Parameter	Dog	Cat
pH	7.35–7.46	7.31–7.46
PCO_2 (mmHg)	31–43	25–37
HCO_3^- (mmol/l)	18–26	14–22
Base excess (BE)	−4 to +2	−4 to +2

5.8 Approximate normal values for acid–base parameters in arterial blood.
(Based on Haskins, 1983)

Respiratory acid–base disturbances

Respiratory acid–base disturbances occur secondary to alterations in the concentration (partial pressure) of carbon dioxide (PCO_2) in the blood. Because carbon dioxide is an acid in solution, an increase in PCO_2 leads to a respiratory acidosis and a decrease in PCO_2 leads to a respiratory alkalosis. As blood levels of carbon dioxide are determined by the state of alveolar ventilation, the causes of respiratory acidosis and alkalosis are identical to those for hypo-and hyperventilation, respectively. These are summarized in Figure 5.9 and discussed in more detail in Chapter 7. In animals with chronic respiratory acid–base disturbances, the kidneys can compensate by altering net acid excretion and bicarbonate resorption. Treatment for respiratory acid–base disturbances involves resolution of the underlying problem or, if severe, intubation with mechanical ventilation to normalize PCO_2. Bicarbonate should not be administered to patients with severe respiratory acidosis. In this situation, bicarbonate is ineffective in improving the acidosis (and may actually worsen acidosis) as the patient is unable to excrete the carbon dioxide formed as the bicarbonate combines with hydrogen ions. Bicarbonate administration also has the theoretical potential to cause several detrimental effects, including worsening hypoxaemia, paradoxical cerebrospinal fluid acidosis and hypotension.

Respiratory acidosis (hypoventilation)
• Upper airway obstruction • Respiratory centre depression • Central neurological disease • Drugs (e.g. anaesthesia) • Neuromuscular disease (e.g. myasthenia gravis, polyradiculoneuritis, botulism) • Restrictive disease (e.g. pneumothorax, pleural effusion) • Respiratory muscle fatigue (e.g. severe parenchymal disease) • Inadequate mechanical ventilation
Respiratory alkalosis (hyperventilation)
• Hypoxaemia (severe) • Pulmonary parenchymal disease • Hyperthermia • Pain • Fear/stress • Exercise • Neurological disease • Excessive mechanical ventilation

5.9 Causes of respiratory acid–base disturbances.

Metabolic acid–base disturbances

Metabolic acid–base disturbances occur as a result of alterations in the non-volatile (i.e. non-carbon dioxide) acids in the blood. A metabolic alkalosis implies that acid has been lost from the body. A metabolic acidosis implies that an acid has been added or generated within the body, or that bicarbonate (the principal buffer) has been lost from the body. The anion gap can be used to help distinguish between these two categories.

Causes of metabolic acid–base disturbances are summarized in Figure 5.10. Respiratory compensation for primary metabolic disturbances occurs rapidly and is often very effective, therefore the plasma pH may be close to normal. Treatment for metabolic acid–base disturbances involves resolution of the underlying problem (e.g. fluid therapy for lactic acidosis, insulin therapy for ketoacidosis). In animals with severe metabolic acidosis (pH <7.2) in which the primary disturbance cannot be resolved quickly, it may be necessary to administer bicarbonate. The bicarbonate deficit is calculated as below:

Bicarbonate deficit = bodyweight (kg) x base excess x 0.3

One-third of the calculated deficit is administered by slow intravenous infusion over 15–30 minutes and the acid–base status is reassessed. If necessary, the remainder can be added to the patient's intravenous fluids and delivered over a period of hours.

Metabolic acidosis

- High anion gap (normochloraemic)
  - *Diabetic ketoacidosis*
  - *Lactic acidosis*
  - *Uraemic acidosis*
  - Toxins (e.g. ethylene glycol, salicylates)
- Normal anion gap (hyperchloraemic)
  - *Diarrhoea*
  - Renal tubular acidosis
  - Drugs (e.g. carbonic anhydrase inhibitors)
  - Dilutional acidosis

Metabolic alkalosis

- Associated with hypochloraemia
  - *Vomiting*
  - *Diuretic therapy*
  - Following hypercapnia
- Not typically associated with hypochloraemia
  - Primary hyperaldosteronism
  - Hyperadrenocorticism

5.10 Causes of metabolic acid–base disturbances. Diagnoses in *italics* are those encountered most frequently in clinical practice.

Interpreting acid–base results

Interpretation of acid–base results involves integrating the information provided by the pH, PCO_2 and base excess (or bicarbonate). All three parameters should be looked at every time an acid–base panel is reviewed. Electrolyte values are also essential for full interpretation, especially of metabolic acidosis. The following points should be used when interpreting acid–base results in clinical patients. Expected patterns are summarized in Figure 5.11.

Disorder	pH	PCO_2	BE	Bicarbonate
Metabolic acidosis	↓	(↓)	Negative	↓
Metabolic alkalosis	↑	(↑)	Positive	↑
Respiratory acidosis	↓	↑	(Positive)	(↑)
Respiratory alkalosis	↑	↓	(Negative)	(↓)

5.11 Expected patterns of acid–base parameter changes in patients with primary acid–base disturbances. Trends in parentheses indicate a compensatory response. BE = base excess.

1. Look at the pH:
   - Is it acidaemic (pH <7.4), alkalaemic (pH >7.4) or normal (pH approximately 7.4)?
2. If acidaemia is present, determine whether it is respiratory or metabolic in origin:
   - If PCO_2 >45 mmHg, there is a primary respiratory acidosis
   - If BE is negative (or bicarbonate <18 mmol/l), there is a primary metabolic acidosis.
3. If alkalaemia is present, determine whether it is respiratory or metabolic in origin:
   - If PCO_2 <33 mmHg, there is a primary respiratory alkalosis
   - If BE is positive (or bicarbonate >24 mmol/l), there is a primary metabolic alkalosis.
4. Following on from point 2 or 3 above, assess whether the patient has evidence of compensation, and whether this appears to be adequate. Expected compensation for primary acid–base disturbances is shown in Figure 5.12. Inadequate compensation may be because there has been insufficient time for compensation, or because there is a second primary acid–base process that is preventing the expected compensation.
5. If pH is normal, look at PCO_2 and BE:
   - If both PCO_2 and BE are abnormal, the patient has either a fully compensated acid–base disturbance or two primary processes that are effectively cancelling each other out. These scenarios can be difficult to distinguish. Clinical information may be helpful. Also remember that overcompensation does not occur. In most patients with a fully compensated acid–base disturbance the pH will be only just within the normal range, and the direction of deviation from 7.4 will indicate the primary process
   - If both PCO_2 and BE are normal, then either the patient is normal or the patient has a primary metabolic acidosis and a concurrent primary metabolic alkalosis. Along with the clinical picture, the patient's electrolytes should help identify the latter group, as they will almost always be hypochloraemic.

Disorder	Primary change	Expected compensatory response
Metabolic acidosis	↓ $[HCO_3^-]$	0.7 mmHg decrease in PCO_2 for each 1 mmol/l decrease in $[HCO_3^-]$
Metabolic alkalosis	↑ $[HCO_3^-]$	0.7 mmHg increase in PCO_2 for each 1 mmol/l increase in $[HCO_3^-]$
Acute respiratory acidosis	↑ PCO_2	1.5 mmol/l increase in $[HCO_3^-]$ for each 10 mmHg increase in PCO_2
Chronic respiratory acidosis	↑ PCO_2	3.5 mmol/l increase in $[HCO_3^-]$ for each 10 mmHg increase in PCO_2
Acute respiratory alkalosis	↓ PCO_2	2.5 mmol/l decrease in $[HCO_3^-]$ for each 10 mmHg decrease in PCO_2
Chronic respiratory alkalosis	↓ PCO_2	5.5 mmol/l decrease in $[HCO_3^-]$ for each 10 mmHg decrease in PCO_2

5.12 Expected renal and respiratory compensation for primary acid–base disturbances in dogs.
(Modified from DiBartola, 2012a)

Examples of acid–base disturbances, explanations of interpretation, and major differential diagnoses to consider are given below.

Example 1

pH 7.48
PCO_2 27 mmHg
BE –1
HCO_3^- 19 mmol/l

Interpretation: acute respiratory alkalosis. The pH is increased, indicating an alkalaemia, and the low PCO_2 confirms that this is a primary respiratory alkalosis. There is no compensation, indicating that it is acute. Common differential diagnoses would include a dog that is stressed, in pain or hyperthermic, or an animal that is hyperventilating to improve oxygenation. If clinically indicated, pulse oximetry or arterial blood gas analysis with assessment of arterial partial pressure of oxygen (P_aO_2) (see Chapter 7) should be performed. ▶

Example 2

pH 7.31
PCO_2 28 mmHg
BE –8
HCO_3^- 12 mmol/l

Interpretation: compensated metabolic acidosis. The pH is decreased, indicating an acidaemia. The negative BE and low bicarbonate confirm that this is a primary metabolic acidosis. The carbon dioxide is decreased in compensation, and the magnitude of the decrease is appropriate. If the abnormal carbon dioxide was the primary process, it would tend to lead to an alkalaemia, which is not present in this patient. An underlying cause for the acidaemia should be sought. Common differential diagnoses include lactic acidosis (with poor perfusion and shock), ketoacidosis or uraemia.

Example 3

pH 7.40
PCO_2 22 mmHg
BE –12
HCO_3^- 10 mmol/l

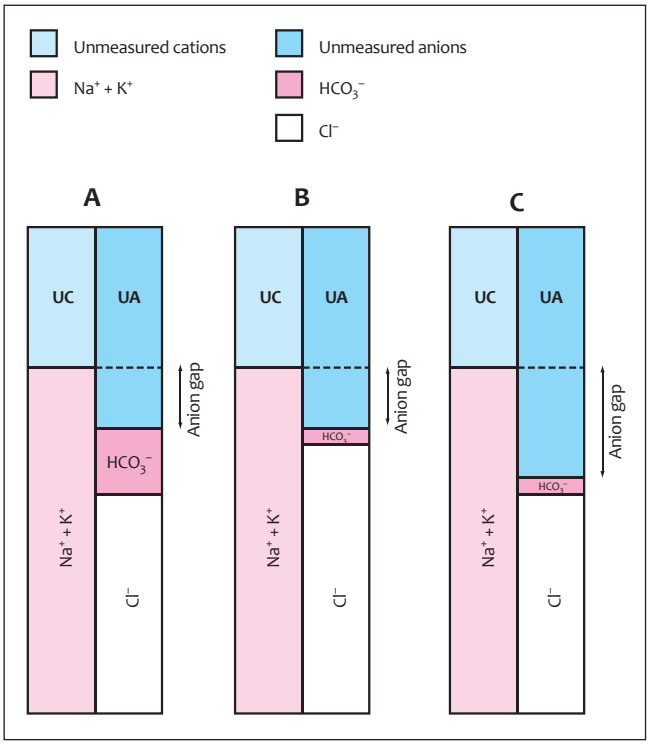
Interpretation: this patient has a normal pH but both the BE/bicarbonate and PCO_2 are very abnormal. The low BE/bicarbonate implies a metabolic acidosis and the low PCO_2 implies a respiratory alkalosis. Considering that the pH is close to the middle of the normal range and the BE/bicarbonate and PCO_2 are more extreme than would be expected for compensation, this is likely to represent two primary processes that are effectively cancelling each other out in terms of pH. The differential diagnosis lists for both metabolic acidosis and respiratory alkalosis should be considered when evaluating a complete problem list for this patient and deciding upon further diagnostic tests and treatment. Treatment aimed at only one of the processes may lead to worsening of the pH as the other process can then predominate.

The anion gap

The anion gap is a concept that can be used to help determine whether a metabolic acidosis was caused by addition of an acid or by loss of bicarbonate. The anion gap is calculated using the following formula:

$$\text{Anion gap} = ([Na^+] + [K^+]) - ([Cl^-] + [HCO_3^-])$$

The body must maintain electroneutrality (i.e. the number of cations in the body must equal the number of anions). The total number of cations in blood includes sodium, potassium and others, for example calcium and magnesium, which are not included in this equation and are therefore termed 'unmeasured'. Similarly, a number of 'unmeasured' anions are not included in this equation, for example sulphates and phosphates. The presence of a small anion gap in normal animals simply tells us that there are more unmeasured anions than unmeasured cations. A normal anion gap is 10–27 in cats and 8–25 in dogs. An acidosis with a normal anion gap implies that no additional unmeasured anions are present in the blood, thus loss of bicarbonate is the cause of the acidosis. Conversely, an acidosis with a high anion gap implies the presence of an unmeasured anion (e.g. lactate, ketones, salicylate) and hence addition or generation of an acid within the body (Figure 5.13). It is now possible to measure many of these unmeasured anions, and hence the usefulness of the anion gap approach is reduced.



5.13 Schematic representation of the use of anion gap for determining the cause of metabolic acidosis. As plasma electroneutrality must be maintained, the total number of cations must equal the total number of anions. (A) A normal dog, in which the anion gap (AG) represents the difference between the unmeasured cations (UC) and the unmeasured anions (UA). (B) A patient with a metabolic acidosis secondary to loss of bicarbonate. As no other anions have been added to the body, chloride is increased so electroneutrality is maintained and the patient has a normal anion gap (or hyperchloraemic) acidosis. (C) A patient in which the acidosis is caused by addition of an acid (i.e. anion) to the body (e.g. lactate or phosphate). This anion is buffered by bicarbonate which decreases, but as another anion is present chloride does not change. This represents a high anion gap (or normochloraemic) acidosis.

Non-traditional acid–base analysis

The value of acid–base analysis in patient care revolves around its ability to enhance diagnosis and treatment of critically ill animals. A major criticism of the traditional approach to acid–base interpretation, as described above, is that even with the use of the anion gap, it does not fully identify disease processes that contribute to a metabolic acid–base disturbance. Further, it does not fully recognize and integrate the fact that changes in electrolytes and proteins have an impact on the acid–base status of the patient. This has led to development of the non-traditional approach to acid–base analysis, also known as the strong ion or Stewart approach.

Put simply, the Stewart approach considers there to be three independent variables that impact acid–base balance: the partial pressure of CO_2 (this is identical to the respiratory component in the traditional approach), the difference between strong (fully dissociated) cations and anions, known as the strong ion difference (SID), and total

weak acids (A_{tot}), which predominantly comprises of albumin and phosphate. Acid–base abnormalities may arise due to changes in any of these three variables.

The traditional approach to acid–base analysis works very well for the majority of patients, however, in some critically ill patients with complex disease processes including changes in protein levels and water balance, the Stewart approach can provide additional insight to the underlying nature and relative severity of their problems. A full explanation of the process and equations used to apply this method to real patients is beyond the scope of this chapter and the interested reader is referred to other sources (Hopper, 2015).

Conclusion

Acid–base disturbances occur frequently in critically ill patients. In many circumstances, treatment of the underlying disease leads to resolution of the acid–base problem, and improvement in pH can be a sign that treatment is succeeding. In more complex cases, an understanding of acid–base physiology and ability to interpret blood gas parameters can lead to improved patient care in terms of both completeness of the diagnostic evaluation and optimization of the treatment plan for that individual patient.

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Chapter 6

Cardiovascular emergencies

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Emergency approach in cases suspected of cardiovascular disease

Patients presenting with cardiovascular emergencies are often unstable and quick decisions are necessary. The following approach is recommended:

1. Obtain a brief and focused history.
2. Perform a rapid and targeted physical examination.
3. Perform a brief echocardiographic examination and electrocardiogram (ECG).
4. Make a presumptive diagnosis allowing decision-making and initiation of therapy/stabilization procedures.

It is important to keep in mind the main causes of cardiovascular compromise in small animals, so that specific features of each condition can be looked for. The clinical signs and main cardiovascular differential diagnoses are summarized in Figure 6.1.

History and initial stabilization

This is an important step in understanding the patient's presenting problem(s) and to guide further diagnostic testing. In an emergency setting the history has to be taken rapidly and efficiently. The following are important questions to ask:

- For how long has the patient had these clinical signs?
- Has a cardiac condition previously been diagnosed?

Clinical signs	Causes	Differential diagnosis
Dyspnoea Tachypnoea	Pulmonary oedema (dogs)	Myxomatous mitral valve disease, dilated cardiomyopathy
	Pleural effusion (dogs)	It is rare for dogs in congestive heart failure (CHF) to present with isolated pleural effusion. When present, it is typically associated with ascites in cases of right-sided CHF or with pericardial effusion in cases of cardiac tamponade
	Pulmonary oedema (cats) Pleural effusion (cats)	Hypertrophic cardiomyopathy, restrictive cardiomyopathy, unclassified cardiomyopathy, dilated cardiomyopathy
Weakness Collapse Syncope	Pericardial effusion (dogs)	Haemangiosarcoma, heart base tumour (chemodectoma), mesothelioma, idiopathic pericarditis
	Bradyarrhythmias	Third-degree atrioventricular block (dogs, cats), sick sinus syndrome (dogs), atrial standstill (dogs)
	Ventricular tachyarrhythmias	Dilated cardiomyopathy (dogs), arrhythmogenic right ventricular cardiomyopathy, (dogs, cats), hypertrophic cardiomyopathy (cats)
	Supraventricular tachyarrhythmias	Dilated cardiomyopathy (dogs), arrhythmogenic right ventricular cardiomyopathy hypertrophic cardiomyopathy (cats), severe myxomatous mitral valve disease (dogs), primary supraventricular tachycardia (dogs, cats)
	Pulmonary hypertension (dogs)	Myxomatous mitral valve disease, lung fibrosis, pulmonary thromboembolism, congenital heart disease causing right-to-left shunt, lungworm (*Angiostrongylus vasorum*), heartworm (*Dirofilaria immitis*)
Abdominal enlargement	Ascites Hepatomegaly	Pericardial effusion, pulmonary hypertension, tricuspid dysplasia, arrhythmogenic right ventricular cardiomyopathy
Cough	Left atrial enlargement (dogs) Pulmonary oedema (dogs)	Myxomatous mitral valve disease, dilated cardiomyopathy (cats rarely cough with pulmonary oedema)
Paresis	Arterial thromboembolism (cats)	Hypertrophic cardiomyopathy, unclassified cardiomyopathy, restrictive cardiomyopathy, dilated cardiomyopathy
Cyanosis	Congenital right-to-left shunt	Reverse patent ductus arteriosus (differential cyanosis), Tetralogy of Fallot, ventricular septal defect with Eisenmenger syndrome
	Severe life-threatening pulmonary oedema	Myxomatous mitral valve disease, dilated cardiomyopathy, feline cardiomyopathies

6.1 Clinical signs, causes and differential diagnoses of the common cardiovascular emergencies in small animals.

- Is the patient currently taking any cardiac or other medications?
- In a cat with dyspnoea/tachypnoea, has the owner noticed the cat coughing? If yes, the problem is more likely to be due to primary respiratory tract disease (e.g. asthma)
- In cats with acute congestive heart failure (CHF), it is common to identify precipitating events such as recent fluid administration, anaesthesia/surgery or cortico-steroid administration; the presence of any precipitating factors in the recent history should be explored
- Has the owner noticed any stridor (harsh, high-pitched respiratory sound), stertor (snoring), nasal discharge or change in meowing/barking? These suggest nasopharyngeal/laryngeal disease
- Exercise intolerance may be associated with CHF in dogs, but this is seldom reported in cats as cats tend to lead relatively sedentary lives. If exercise intolerance has been observed, has the owner noticed a bluish tongue (cyanosis) during exercise? This may be consistent with severe pulmonary oedema or cyanotic congenital heart disease, but in these cases the exercise intolerance would also be associated with exertional dyspnoea. Primary respiratory diseases such as severe lung disease or upper airway obstruction may also cause cyanosis
- Possible onset of abdominal distension should be evaluated; it is worth enquiring whether the patient has gained weight in the last 2–3 weeks, as free fluid causing abdominal distension is often perceived by the owner as a rapid, recent weight gain
- In a patient presented for syncope/collapse, a clear description of the event is vital. Differentiation from a seizure may be very difficult or impossible based solely on the history from the owner, but there are some typical clinical features that may help to make the distinction. The following questions are important to ask:
  - What happened just before the event? Events occurring during/after exercise, coughing or stress are likely to be syncopal; on the other hand, prodromal signs (changes in behaviour, attitude) are suggestive of seizure
  - What happened during the event? During a syncopal episode the patient is generally flaccid, while during a seizure the patient may be rigid (tonic), have tonic–clonic movements, may void urine/faeces, salivate and may vocalize. However, it should be borne in mind that a syncopal event may occasionally be characterized by opisthotonos, extensor rigidity, voiding of urine and vocalization. Cats with syncope may even show focal facial clonic movements resembling seizures, making the diagnosis quite challenging
  - How did the dog/cat recover from the event? A rapid recovery suggests syncope, while a slow, protracted recovery with disorientation and behavioural changes is more typical of a seizure. The typical syncopal episode is characterized as a short loss of postural tone and consciousness, which is induced by stressful situations or exercise, with spontaneous and rapid recovery. There are cases in which differentiation from a seizure may be difficult, such as when a longer syncopal episode induces a hypoxic seizure. In these cases, the precise description of the first part of the event, which will be characterized by flaccid collapse, is important so that syncope is still considered and specific work-up is performed
  - How long did the event last? This can be a difficult question for the owner to answer because, at the time, the owner is distressed and anxious and therefore may find it difficult to assess time accurately. Framing the question in a specific way, such as 'Did the event last less than 1 minute or around 5 minutes?', may help the owner to have a better perception of time and help the clinician to understand how long the event lasted. Syncopal episodes are usually short (less than 30 seconds and typically less than 10 seconds).

Although history taking is presented here as the first step in the approach to a cardiovascular emergency, this is not always possible. In an unstable patient (e.g. severe dyspnoea, collapse), a quick physical examination and initial measures to stabilize the patient may need to precede the history. If the patient is presented in lateral recumbency or has collapsed shortly before presentation, a more useful approach would be a rapid physical examination followed immediately by a short echocardiogram and ECG (see U-SEE approach below). A dyspnoeic patient will benefit from receiving oxygen, ideally in an oxygen cage in the emergency room where it can be observed while the history is being taken. In a large-breed dog where this may not be possible, flow-by or mask oxygen may be adequate.

It should be borne in mind that even minimal handling of these unstable patients can cause life-threatening respiratory decompensation. The prompt administration of oxygen and potentially cautious sedation are key. It is important not to try to do too much at once and to allow the unstable patient to have periods between procedures where it can become calm in an oxygen-enriched environment. In these cases, sedation can also be very useful to minimize the patient's stress and facilitate initial examination and stabilization. Although sedation may affect heart rate, myocardial contractility, ventricular wall thickness and systemic blood pressure, some protocols are relatively safe and will not affect echocardiographic and electrocardiographic variables in a clinically significant way (Figure 6.2). However, care must be taken to monitor respiratory function in all sedated patients, as some protocols that are safe with regard to cardiovascular function can cause mild respiratory depression. If respiratory function is borderline, this can be sufficient to precipitate respiratory decompensation. Clinicians should be prepared to monitor and if necessary intubate and provide respiratory support to all sedated patients.

Physical examination

The physical examination should be fast and targeted. When the patient is not in an immediately life-threatening state, a short period of time should be taken to observe the animal's breathing pattern and to count the respiratory rate before handling. In patients with abnormal breathing, the physical examination should be performed carefully and with minimal restraint. This is especially important in dyspnoeic cats, as stress can rapidly lead to a life-threatening situation. The patient should be assessed with the goal of finding signs suggestive of a cardiovascular abnormality and evaluating the best means of acute stabilization. The key components of a rapid examination of the cardiovascular system are to check the colour of the oral mucous membranes, perform lung and heart auscultation, assess jugular veins, perform abdominal palpation (soft and gentle; avoid if the patient is dyspnoeic), assess femoral pulses, and then

Drug	Dosage	Comments
Light sedation		
Butorphanol (dogs and cats)	0.2–0.3 mg/kg i.v., i.m.	Short duration of sedation in anxious (but not fractious or aggressive) patients
Butorphanol (B) + acepromazine (ACP) (dogs)	0.2–0.3 mg/kg i.v., i.m. (B) + 0.01–0.02 mg/kg i.v., i.m. (ACP) Lower doses of ACP required in large-breed dogs and Boxers: 0.005–0.01 mg/kg i.v., i.m.	Needs relaxed period of time to work effectively
Butorphanol (B) + midazolam (M) (dogs)	0.2–0.3 mg/kg i.v., i.m. (B + M)	
Deeper sedation in cats		
Ketamine (K) + midazolam (M)	1.0–2.5 mg/kg i.v., orally (K) in severely fractious cats or 3.0–5.0 mg/kg i.m. (K) + 0.2–0.3 mg/kg i.v., i.m. (M)	Profound sedation lasting 15–20 minutes
Ketamine (K) + acepromazine (ACP) + butorphanol (B)	1.5 mg/kg i.v. (K) + 0.02 mg/kg i.m. (ACP) + 0.25 mg/kg i.m. (B)	Ketamine increases heart rate, which may be detrimental in cats with outflow tract obstruction and diastolic disfunction
Butorphanol (B) + alfaxalone (A)	0.2 mg/kg i.m. (B) + 1.0–2.0 mg/kg i.m. (A)	Deep sedation useful for fractious or aggressive patients

6.2 Sedation protocols in cardiovascular emergencies.

check rectal/penile/vaginal mucous membrane colour. Pale mucous membranes suggest anaemia or peripheral vasoconstriction. Anaemia is an important differential diagnosis as it may mimic primary cardiovascular disease by inducing tachypnoea, a heart murmur and cardiomegaly on radiography/echocardiography.

Findings suggestive of underlying heart disease include the presence of a heart murmur, arrhythmias, gallop sounds, jugular distension/pulsation, restrictive respiratory patterns and abnormal lung auscultation (e.g. muffled respiratory sounds ventrally, which may be suggestive of pleural effusion (not necessarily due to CHF), and pulmonary crackles). Cardiac auscultation is in general very helpful in dogs to rule in or out relevant heart disease. Dogs presenting with CHF secondary to myxomatous mitral valve disease (MMVD) have a loud systolic left apical heart murmur (grade III/VI or louder). Dogs presenting with dilated cardiomyopathy (DCM) and CHF may be more challenging to diagnose based on cardiac auscultation findings. Not all dogs with DCM have a heart murmur, but, if present, it is typically a soft left apical systolic murmur. A gallop sound (S3) or arrhythmia may also be detected in dogs with DCM. In cats, cardiac auscultation may be completely unremarkable, even with significant underlying structural heart disease and overt heart failure. It is also important to remember that some cats with structurally normal hearts may have a non-pathological, physiological flow murmur. More useful auscultation findings in cats are gallop sounds and arrhythmias. Heart rate may be helpful in dogs to assess the likelihood of CHF; patients with normal heart rates and sinus arrhythmia are unlikely to be in CHF. In cats, heart rate is a less useful indicator in this respect as many cats presented to an emergency clinic have stress-related tachycardia and some cats with heart failure have a normal or low heart rate. Lung auscultation may be unremarkable even in the face of radiographically evident lung oedema; crackles are not always present and in fact most of the time will not be detected. Instead, increased bronchovesicular sounds may be the only abnormality. It is also important to remember that crackles are not specific for lung oedema and may be detected in patients with pneumonia, pulmonary haemorrhage (especially contusions post-trauma) and lung fibrosis.

In cases presenting for collapse/weakness, a careful cardiac auscultation and pulse evaluation should be performed to evaluate for paroxysmal arrhythmias, sustained bradycardia or tachycardia (most frequent causes of syncope are severe bradyarrhythmias or tachyarrhythmias), pulse deficits, muffled heart sounds and/or weak pulses. The last two signs are suggestive of pericardial effusion. If the owner describes rear limb weakness rather than generalized weakness, the femoral pulses should be checked to determine whether they are palpable bilaterally, with equal strength; if not, aortic thromboembolism should be considered. Most cases of distal aortic thromboembolism in cats present with overt paresis or paralysis. A reverse patent ductus arteriosus (PDA) (right-to-left shunt) may present as posterior weakness, and it is important to evaluate mucous membrane colour in the cranial and caudal mucosae for differential cyanosis (pink oral mucosa, bluish penile/vaginal mucosa).

In patients presenting with abdominal distension, the jugular veins should be evaluated for pulsation/congestion (clipping or wetting the fur over the jugular groove in the neck will help with this assessment). The patient should also be examined for the presence of hepatomegaly and/or ascites (fluid wave by abdominal percussion). The presence of all three signs is suggestive of right-sided CHF.

To assess the presence/type of cough, the trachea may be gently palpated. The most frequent cause of cough associated with heart disease is compression of the left mainstem bronchus by an enlarged left atrium (± bronchomalacia), typically seen with MMVD. Lung oedema *per se* does not necessarily induce cough. Cats rarely cough due to pulmonary oedema, although they may open-mouth breathe.

Urgent standing echocardiogram and electrocardiogram (U-SEE)

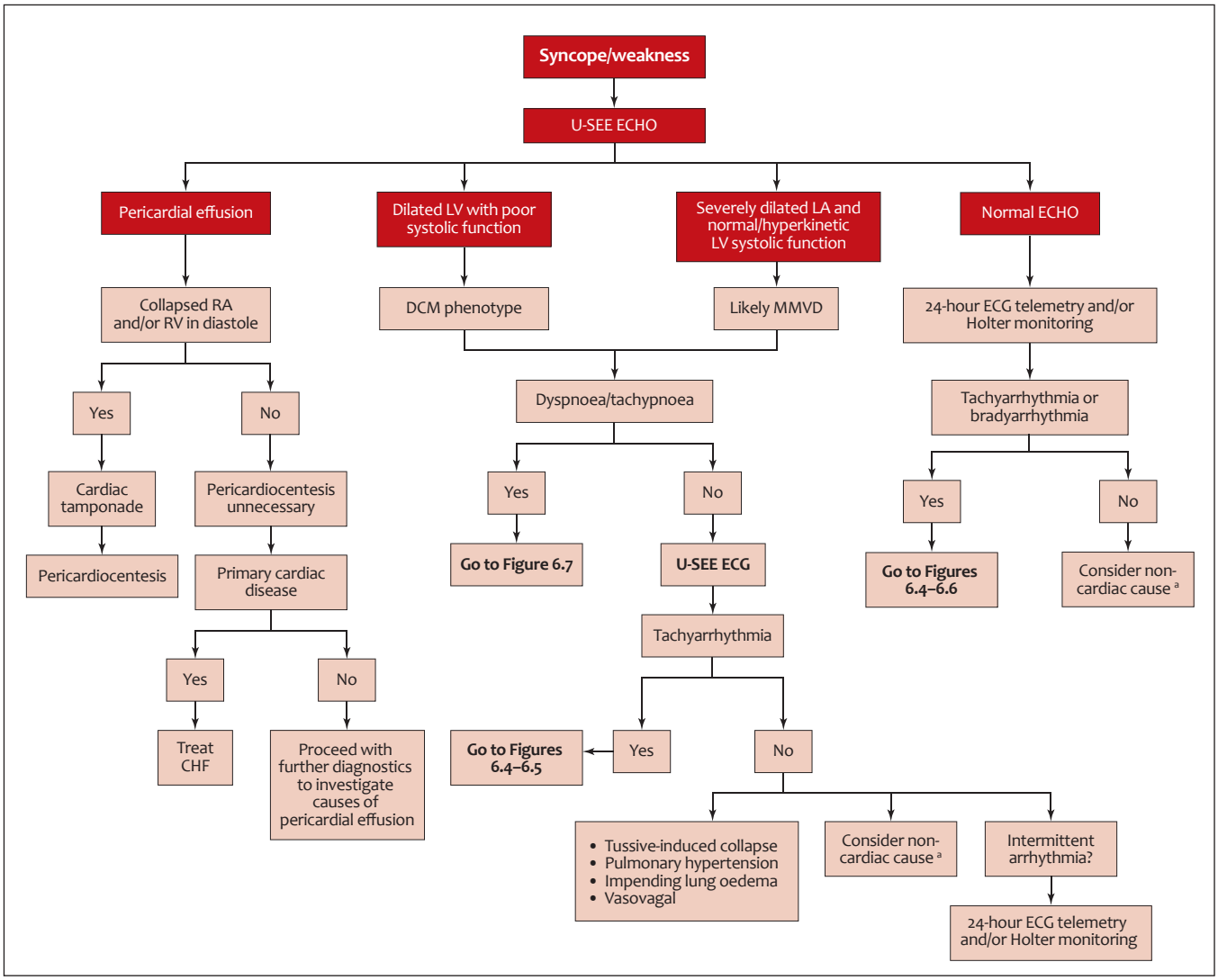
Focused ultrasonography in an emergency setting is widely used in human medicine, and is gaining popularity in veterinary medicine. Ultrasound machines are increasingly available, and with some basic knowledge a large amount of useful information may be gathered with minimal patient manipulation, restraint and stress. Focused ultrasonography in emergency cases was first used in trauma

patients (thoracic/abdominal focused assessment with sonography for trauma (tFAST/aFAST); see Chapters 1 and 24), but has evolved as a useful screening tool for non-trauma patients as well. In veterinary medicine, an additional focused thoracic ultrasound examination has been proposed for patients with respiratory distress, the VetBlue lung scan (Lichtenstein and Meziere, 2008).

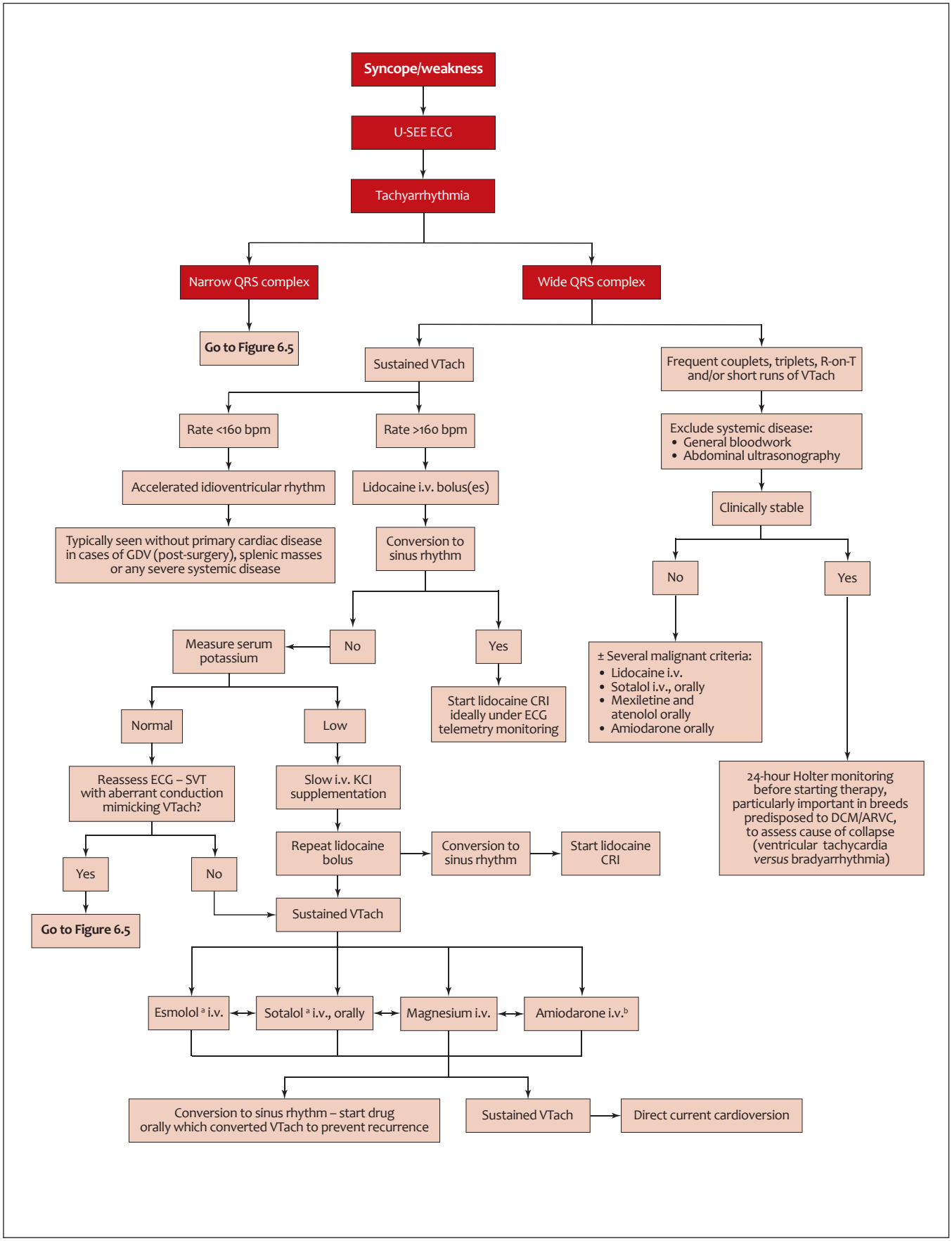
In addition to the very brief assessment performed as part of the FAST scan, a more comprehensive echocardiographic examination can be undertaken in the emergency room. Focused cardiac ultrasound (FOCUS) is indicated in humans in several clinical scenarios, such as dyspnoea, cardiac trauma, hypotension/shock and cardiac arrest (Labovitz *et al*., 2010). Based on the protocols already described for emergency ultrasonography, the authors have proposed a more comprehensive approach combining echocardiography and electrocardiography for the assessment of a suspected cardiovascular emergency.

Urgent standing echocardiogram and electrocardiogram (U-SEE) evaluation is suggested as the initial step in the approach to any patient presenting as a cardiovascular emergency. The aim is to provide a fast and efficient screening examination in the emergency room, allowing assessment of whether the cause of the presenting clinical signs is cardiogenic in origin. The U-SEE assessment is divided into two parts: a brief echocardiographic examination and a lead II ECG, both of which are performed with the patient standing or in sternal recumbency. The evaluation should be performed with minimal restraint and in the position that seems the most comfortable and least stressful for the patient. The short echocardiographic examination cannot and is not intended to replace a comprehensive echocardiographic evaluation. The aim is to evaluate whether the presenting complaints are caused by primary cardiac disease and to decide the best therapy or procedure to stabilize the patient. In the large majority of cardiovascular emergencies a definitive diagnosis (i.e. 'the name of the disease') is not needed for initial emergency therapy. For a definitive diagnosis, comprehensive echocardiography will be needed once the patient has been stabilized.

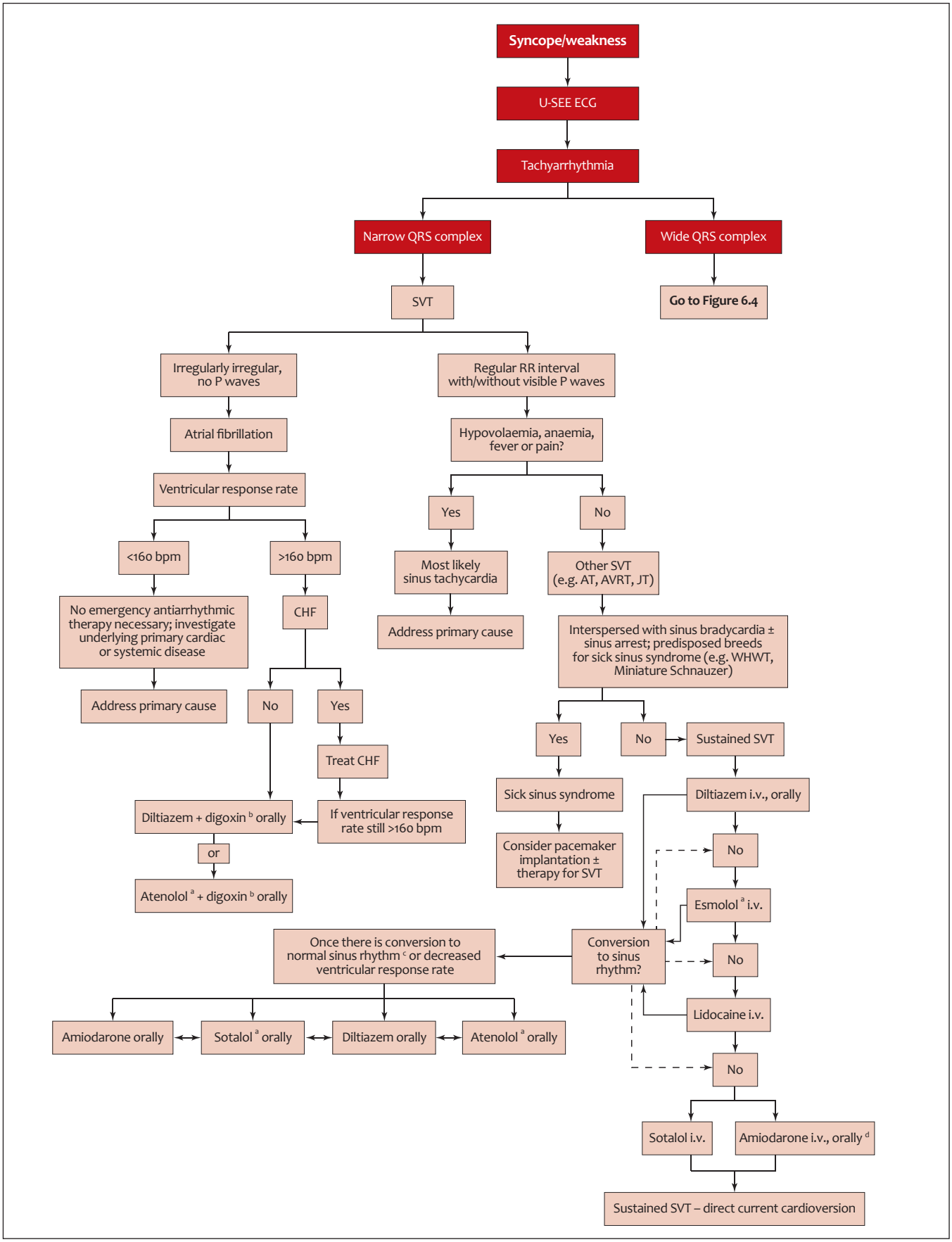
While performing U-SEE, it is important to keep in mind the physical examination findings and the most frequently encountered types of canine and feline heart diseases; this will help focus the examination, making it faster and more efficient (Figures 6.3 to 6.9). U-SEE is intended to be



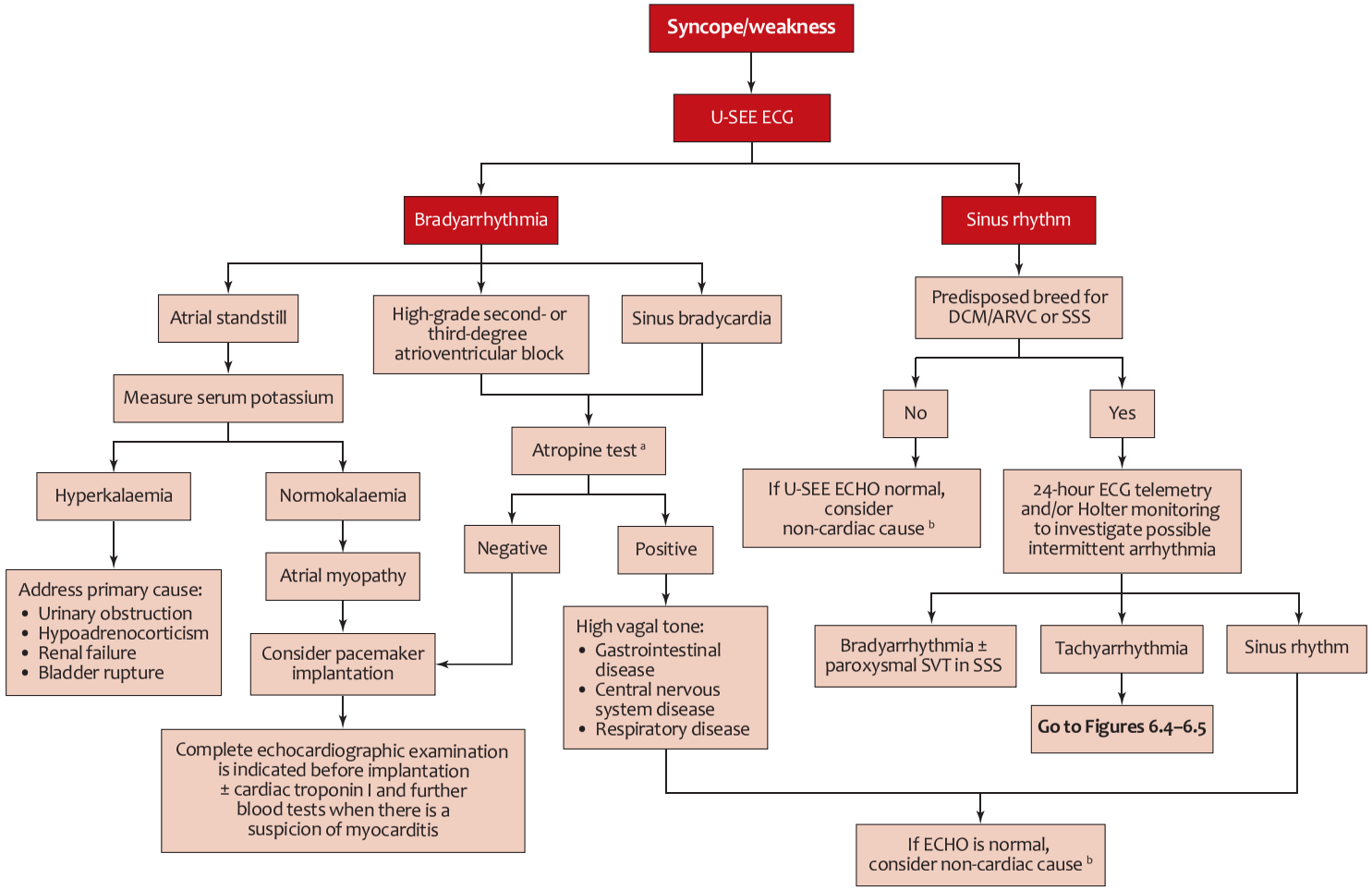
6.3 U-SEE general approach in dogs with syncope/weakness. [a] If all the previous tests are within normal limits, metabolic causes of syncope should be checked. Serum glucose ± fructosamine, haematocrit and electrolytes (sodium, potassium, chloride) ± basal cortisol should be measured to evaluate for hypoglycaemia, anaemia and suspicion of hypoadrenocorticism, respectively. Neurological causes of weakness/seizures should also be considered. CHF = congestive heart failure; DCM = dilated cardiomyopathy; ECG = electrocardiogram; ECHO = echocardiogram; LA = left atrium; LV = left ventricle; MMVD = myxomatous mitral valve disease; RA = right atrium; RV = right ventricle. These presentations are less common in cats. Causes for syncope/weakness in cats are detailed in Figure 6.1.



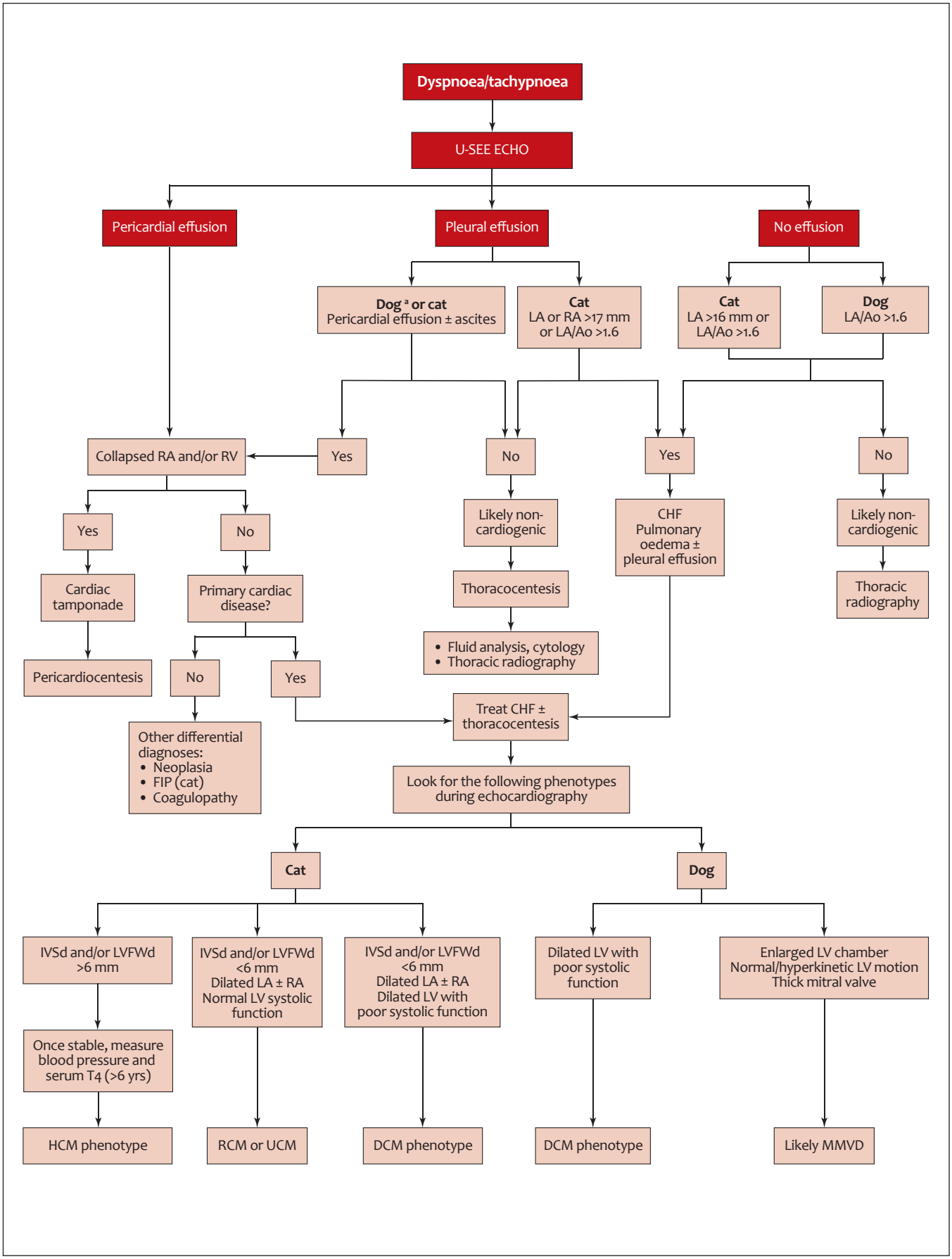
6.4 U-SEE approach in dogs with syncope/weakness and wide complex tachycardia. For details of recommended doses, see Figure 6.32. [a] Avoid if systolic dysfunction (hypokinetic left ventricle) evident on U-SEE echocardiography. [b] Only use intravenous solutions without polysorbate 80, as this may cause anaphylatic reactions. See text for further details. ARVC = arrhythmogenic right ventricular cardiomyopathy; CRI = constant rate infusion; DCM = dilated cardiomyopathy; ECG = electrocardiogram; ECHO = echocardiogram; GDV = gastric dilatation–volvulus; SVT = supraventricular tachycardia; VTach = ventricular tachycardia. These presentations are less common in cats. Causes for syncope/weakness in cats are detailed in Figure 6.1.



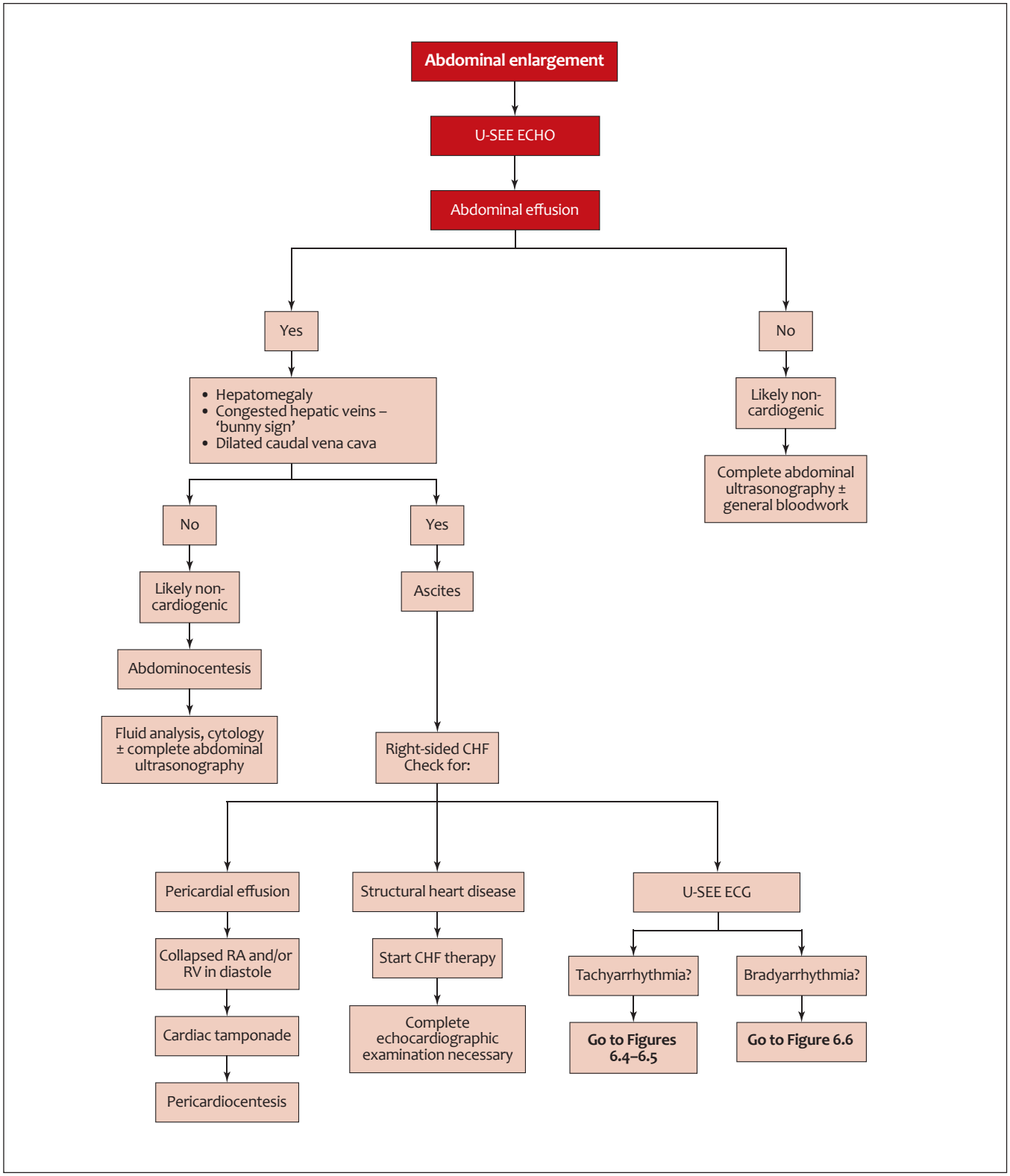
6.5 U-SEE approach in dogs with syncope/weakness and narrow complex tachycardia. For details of recommended doses see Figure 6.32. [a] Avoid if systolic dysfunction (hypokinetic left ventricle) evident on U-SEE echocardiography. In advanced cases of myxomatous mitral valve disease, do not use beta-blockers. [b] Use with caution in cats. [c] Oral administration of one of these drugs is indicated to prevent recurrence of the arrhythmia. [d] Only use intravenous solutions without polysorbate 80, as this may cause anaphylatic reactions. See text for further details. AT = atrial tachycardia; AVRT = atrioventricular reciprocating tachycardia; CHF = congestive heart failure; ECG = electrocardiogram; JT = junctional tachycardia; SVT = superventricular tachycardia; WHWT = West Highland White Terrier. These presentations are less common in cats. Causes for syncope/weakness in cats are detailed in Figure 6.1.



6.6 U-SEE approach in dogs with syncope/weakness and bradyarrhythmias or sinus rhythm. [a] Administer 0.04 mg/kg atropine s.c. and repeat electrocardiogram (ECG) in 30 minutes. A positive response to atropine is considered to be resolution of the atrioventricular block and an increase in heart rate to >160 bpm. [b] If all the previous tests are within normal limits, metabolic causes of syncope should be checked. Serum glucose ± fructosamine, haematocrit and electrolytes (sodium, potassium, chloride) ± basal cortisol should be measured to evaluate for hypoglycaemia, anaemia and suspicion of hypoadrenocorticism, respectively. Neurological causes of weakness/seizures should also be considered. ARVC = arrhythmogenic right ventricular cardiomyopathy; DCM = dilated cardiomyopathy; ECG = electrocardiogram; ECHO = echocardiogram; SSS = sick sinus syndrome; SVT = supraventricular tachycardia. These presentations are less common in cats. Causes for syncope/weakness in cats are detailed in Figure 6.1.



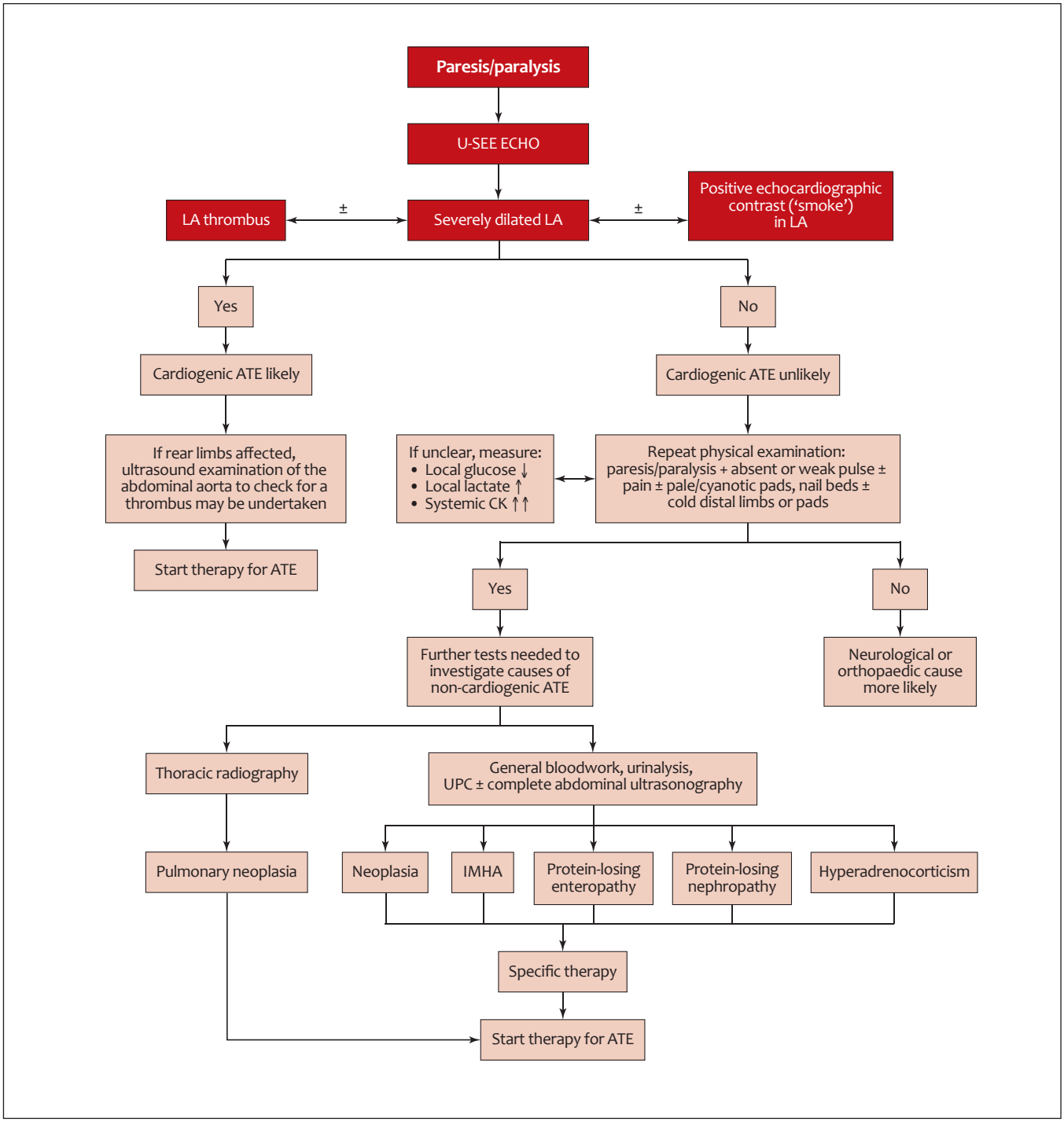
6.7 U-SEE approach in patients with dyspnoea/tachypnoea. [a]It should be noted that it is rare for dogs in congestive heart failure (CHF) to present with isolated pleural effusion. When present, it is almost always associated with ascites in cases of right-sided CHF or with pericardial effusion in cases of cardiac tamponade. Ao = aorta; DCM = dilated cardiomyopathy; FIP = feline infectious peritonitis; HCM = hypertrophic cardiomyopathy; IVSd = interventricular septum in diastole; LA = left atrium; LV = left ventricle; LVFWd = left ventricular free wall in diastole; MMVD = myxomatous mitral valve disease; RA = right atrium; RCM = restrictive cardiomyopathy; RV = right ventricle; UCM = unclassified cardiomyopathy.



6.8 U-SEE approach in patients with abdominal enlargement. CHF = congestive heart failure; ECG = electrocardiogram; RA = right atrium; RV = right ventricle.

performed by all practitioners undertaking emergency work, not only by cardiologists, although a good basic knowledge of cardiology, echocardiography and electrocardiography will be necessary. To help acquire the skills necessary to perform a good U-SEE examination, it is imperative to gain experience in patients with normal cardiovascular status, to become familiar with normal cardiac dimensions and function.

If an ultrasound machine is not available, thoracic radiographs should be taken as a matter of urgency (when the patient is sufficiently stable) to evaluate cardiac size, the pulmonary vessels, the caudal vena cava and the pulmonary parenchyma. Radiographs are very helpful and in certain cases will be necessary to reach a diagnosis and plan therapy (see below for specific radiographic images and descriptions).



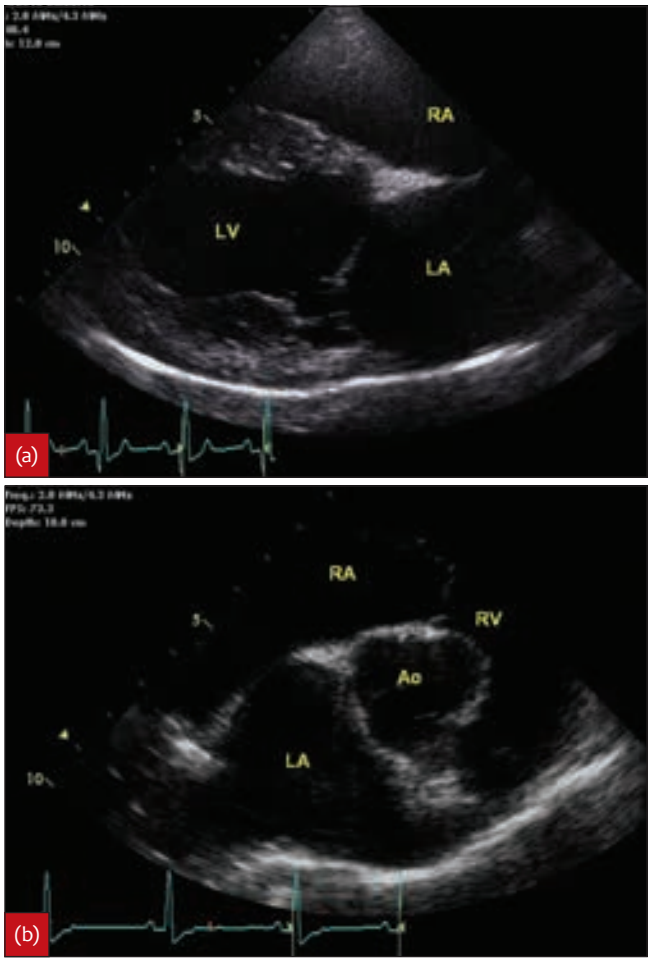
6.9 U-SEE approach in patients with paresis/paralysis. ATE = arterial thromboembolism; CK = creatine kinase; IMHA = immune-mediated haemolytic anaemia; LA = left atrium; UPC = urine protein:creatinine ratio.

U-SEE echocardiography

An echocardiographic examination performed in the emergency room should be short and targeted so that as much information as possible is gathered without compromising the patient. The U-SEE echocardiographic examination comprises four different views/regions, each with specific goals. The first two views aim to assess the heart and the last two views the thoracic and abdominal cavities.

First, a right parasternal long-axis (RPLA) four-chamber view (Figure 6.10a) should be acquired to evaluate the atria, atrioventricular (AV) valves, ventricles and pericardial space. Next, a right parasternal short-axis (RPSA) view at the level of the heart base (Figure 6.10b) should be acquired to assess the left atrium (LA) and pericardial space.

With these two views, it is important to begin by subjectively assessing the dimensions and function of the cardiac chambers, before starting to take measurements. Echocardiographic measurements are prone to error and may have a large inter- and intra-operator variability, especially in less experienced hands. Thus, before taking any measurements, the quality of the echocardiographic image should be optimized. Particular attention should be paid to cardiac chamber size, independently and in relation to the other cardiac chambers, how strong/vigorous is the ventricular myocardial contraction, the thickness of the ventricular walls,



6.10 (a) Right parasternal long-axis four-chamber view in a normal dog at end-systole just before mitral valve opening. From this view it is possible to assess the atria, atrioventricular valves, ventricles and pericardial space. (b) Right parasternal short-axis view at the level of the heart base in a normal dog at end-systole before aortic valve opening (i.e. just after the T wave on the ECG). From this view it is possible to assess the left atrium (size, presence of 'smoke', thrombus) and pericardial space. Ao = aorta; LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ventricle.

the appearance of the AV valves (i.e. do they open properly, do they look thick?) and if there is any fluid around the heart. The subjective impression of cardiac dimensions and function is the most important assessment in an emergency scenario. There is no need for complex measurements of function or dimension; basic measurements should serve to confirm the first impression of the clinician.

The thorax and abdomen should be evaluated for pleural and abdominal effusion, respectively. For clinicians with more advanced ultrasonography expertise, the liver should be assessed for signs of venous congestion, and in cases of suspected arterial thromboembolism, the terminal abdominal aorta can be evaluated for the presence of a thrombus.

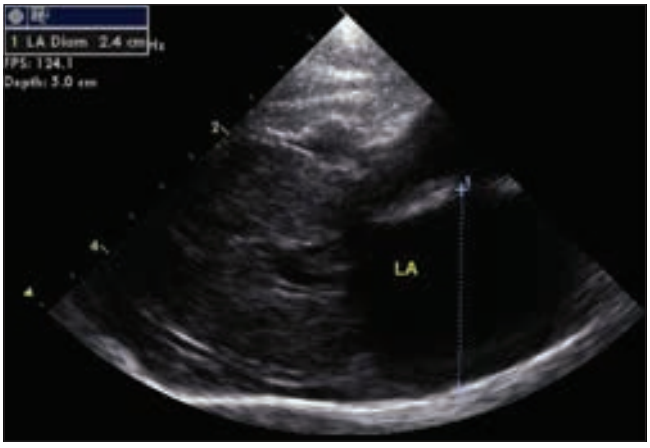
Atrial assessment: Atrial size is one of the most important parameters to be assessed during U-SEE echocardiography. Atrial enlargement reflects increased ventricular filling pressures, which indicates the severity and chronicity of heart disease, and importantly, the clinical relevance of the cardiac disease to the presenting signs of the patient.

In cats presented for dyspnoea, LA dimension has been shown to be a very good parameter to distinguish between left-sided CHF and respiratory disease. A LA dimension >17 mm is associated in the majority of cases with left-sided CHF (Smith and Dukes-McEwan, 2012). In cats, the LA may be measured on either a RPLA or RPSA view. On the RPLA view, the diameter of the LA is measured parallel to the plane of the mitral valve annulus, dissecting the atrium into two equal halves. This measurement is taken at end-systole (i.e. just before mitral valve opening). The cursor should measure the atrium from the interatrial septum to the free wall (anteroposterior dimension) (Figure 6.11). The right atrium (RA) can be measured in a similar fashion and using the same cut-off values.

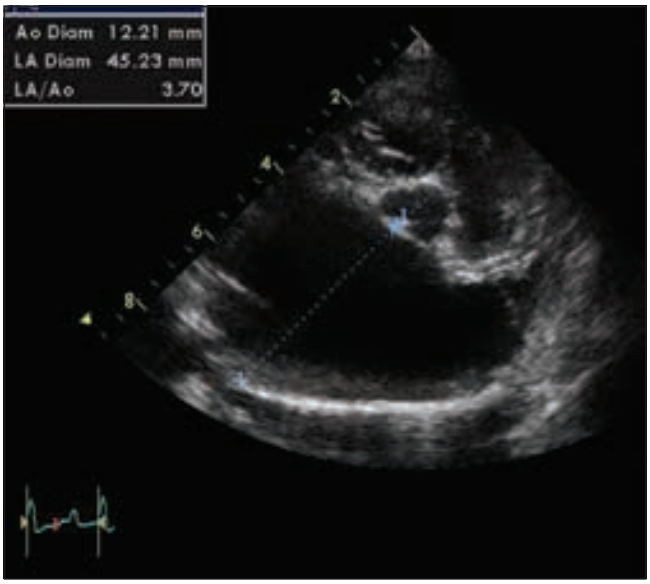
In dogs, a RPSA view is preferable for assessing LA size because the LA can be compared with the size of the aorta (Ao) to give a dimensionless measurement (or ratio), so that breed-specific values are not necessary. A normal LA/Ao ratio is <1.6. The aortic diameter should be measured by drawing a line from the commissure between the left coronary and non-coronary cusps to the middle of the right coronary cusp, and the LA size can be measured by extending this line to the edge of the atrial free wall (Figure 6.12). The RPSA view can be used in the same manner in cats to assess LA size.

The LA is significantly enlarged in almost all cases of left-sided CHF (i.e. dogs presenting with lung oedema, and cats presenting with lung oedema and/or pleural effusion). Uncommon exceptions include acute rupture of the major chordae tendineae supporting the mitral valve leaflets in dogs with previously mild MMVD and in cats whenever a patient with compensated heart disease is exposed to an acute event, such as large volumes of fluid therapy. In both situations the LA does not have time to significantly dilate and may be only mildly dilated at presentation. These exceptions can usually be diagnosed by echocardiographic evaluation of the mitral valve movement/morphology in the first case and a detailed recent history in the second. In cases of mitral valve chordal rupture, the leaflets display a chaotic movement, resulting in the free edge of the valve leaflet (usually the anterior mitral valve leaflet) pointing back into the LA during systolic closure (i.e. flail leaflet) (Figure 6.13).

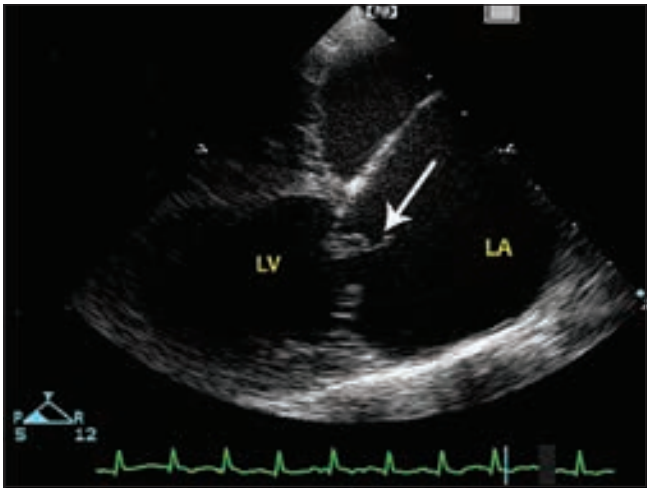
In addition to size assessment, the atria should be evaluated for the presence of spontaneous echocardiographic contrast ('smoke'). This is a risk factor for thrombosis and is a very important finding along with atrial



6.11 Right parasternal long-axis four-chamber view in a cat with hypertrophic cardiomyopathy (obtained just before mitral valve opening). The atria can be assessed using this view. The measurement should be obtained parallel to the mitral or tricuspid valve annulus, dissecting the atrium into two equal parts. The cursor should be placed in the interatrial septum and a line drawn to the atrial free wall. In this case, the left atrium (LA) was measured and shown to be dilated at 24 mm (normal <16 mm).



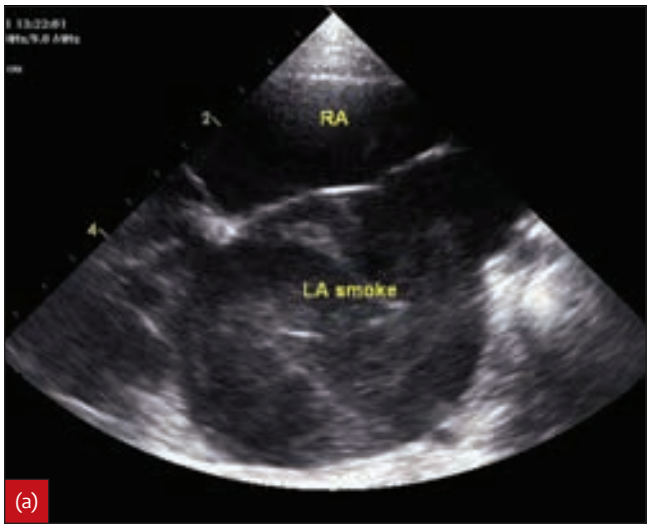
6.12 Right parasternal short-axis view at the level of the heart base in a dog with myxomatous mitral valve disease and severe left atrial dilatation. This view can be used to measure the dimension of the left atrium (LA) in both dogs and cats. In the first instance the aorta (Ao) should be measured by drawing a line from the commissure between the left coronary cusp and the non-coronary cusp to the middle of the right coronary cusp. In this case, it measured 12.21 mm. The LA size is measured by extending this line to the edge of the atrial free wall. In this case, the dimension of the LA measured 45.23 mm. The LA/Ao ratio was determined to be 3.70 (normal LA/Ao ratio is <1.6).

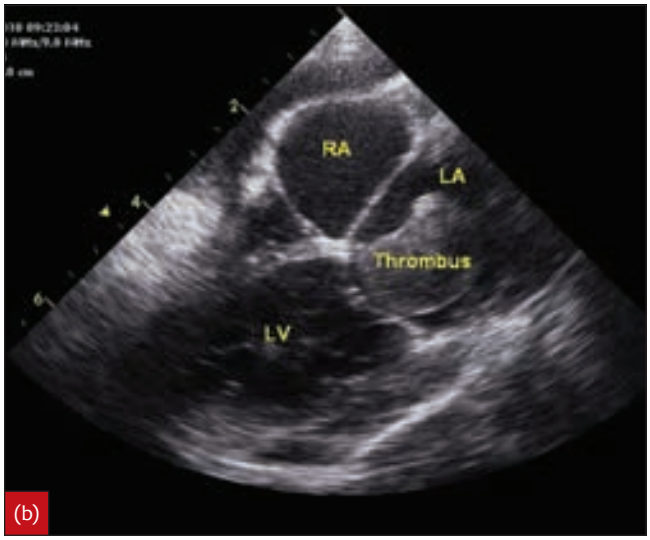


6.13 Right parasternal long-axis four-chamber view in a dog with myxomatous mitral valve disease and rupture of a primary mitral valve chorda tendinea. In cases of major chordal rupture, the affected valve leaflet will display a chaotic 'flailing' movement and the ruptured chorda is displaced into the left atrium (LA) when the mitral valve closes in systole (arrowed). LV = left ventricle.

dilatation in a patient with sudden-onset limb paresis/paralysis. In some cases, a thrombus can be seen within the left heart chambers (typically the LA or left auricular appendage) (Figure 6.14).

Ventricular assessment: The left ventricle (LV) should be evaluated using a RPLA and/or RPSA (papillary muscle level) view. The main features to be assessed are the presence of eccentric or concentric hypertrophy and ventricular kinesis/movement. The most common causes of left-sided CHF in dogs are MMVD and DCM. In both cases the LV will be volume overloaded, although with mitral valve disease the ventricle is hyperkinetic, whereas with DCM it is hypokinetic.



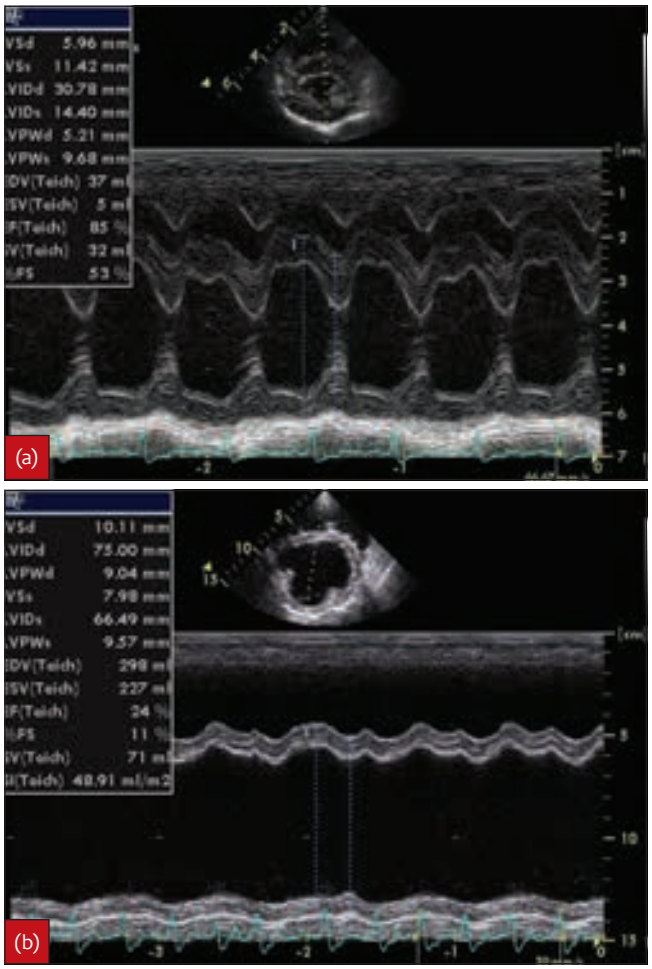


6.14 Right parasternal long-axis four-chamber views in two cats with restrictive cardiomyopathy. (a) A large amount of spontaneous echocardiographic contrast is visible in the left atrium (LA). In real-time this is seen as 'smoke' (i.e. spontaneous echocardiographic contrast) swirling around the atrium. This is typically seen in severely dilated atria and is a marker of increased thromboembolic risk. (b) A large thrombus is seen inside the LA. LV = left ventricle; RA = right atrium.

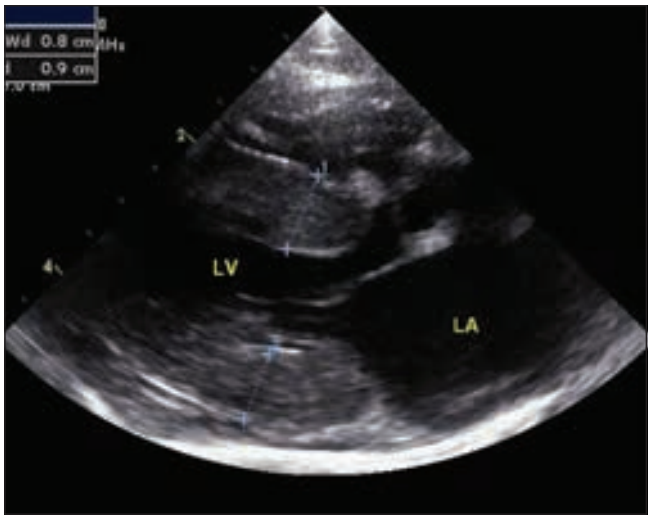
If a more objective measurement is desired, an M-mode image just below the level of the mitral valve can be obtained to assess LV motion through calculation of fractional shortening (FS, expressed as a percentage). The M-mode cursor should transect the ventricle perpendicularly. A hyperkinetic ventricle will show FS above the normal range (>45%), whilst a significantly hypokinetic ventricle will have values <15%. Care should be taken in cases where the image is suboptimal as FS assessment is highly prone to error and, as previously mentioned, the subjective impression alone is highly reliable to a trained eye (Figure 16.15).

Hypertrophic cardiomyopathy (HCM) is the most common cause of feline CHF and/or arterial thrombosis. In these cases, the LV wall will be markedly thickened (Figure 6.16). The wall thickness should be measured at end-diastole (just after mitral valve closure) and the thickest segments should be chosen for measurement. Values >6 mm are considered abnormal. It is important to emphasize that false-positive results can be easily obtained from suboptimal (oblique) images.

In restrictive cardiomyopathy (RCM), both atria are severely dilated, with LV wall thicknesses appearing



6.15 Left ventricular (LV) M-mode image acquired from a right parasternal short-axis view at the level of the papillary muscles in a dog with (a) myxomatous mitral valve disease and (b) dilated cardiomyopathy (DCM). These are two examples of LV eccentric hypertrophy but with marked differences in myocardial systolic function. Note the (a) hyperkinetic LV motion, which is typically associated with mitral regurgitation, and (b) the hypokinetic LV motion, which defines a DCM phenotype.

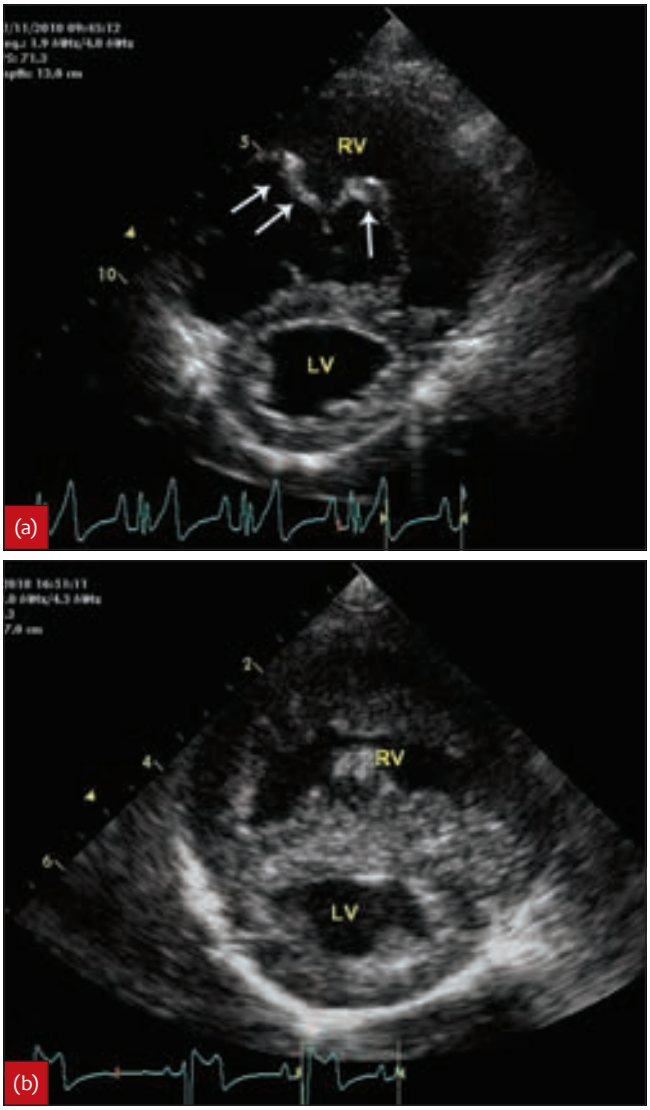


6.16 Right parasternal long-axis four-chamber view in a cat with hypertrophic cardiomyopathy. There is severe ventricular hypertrophy (normal left ventricular wall thickness in diastole is <6 mm; in this case LV walls measured 8–9 mm). The left ventricular wall should be measured at end-diastole (just after mitral valve closure) and the thickest segments should be chosen for measurement. LA = left atrium; LV = left ventricle.

normal and systolic function apparently maintained. There is a subtype of RCM called the endomyocardial form, in which a fibrotic (scar) bridging band may be seen crossing the LV chamber with variable degrees of mid-ventricular focal thickening. Feline DCM cases are rare and characterized by a hypokinetic and volume overloaded LV.

The right ventricle (RV) should be assessed using a RPLA and/or RPSA view at the level of the papillary muscles. The two most frequent causes of RV eccentric hypertrophy are tricuspid dysplasia (Figure 6.17a) and moderate to severe pulmonary hypertension (in the latter, some degree of concentric hypertrophy is expected as well). Marked LV or RV concentric hypertrophy is more frequently seen in congenital heart diseases, namely subaortic and pulmonic stenosis (Figure 6.17b), respectively.

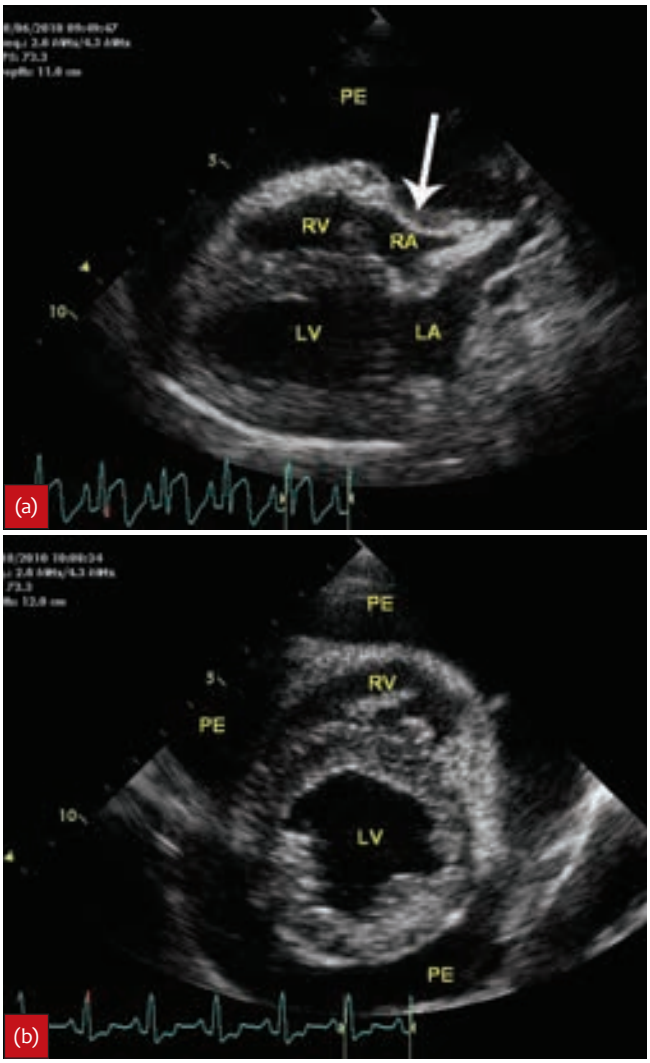
When U-SEE is performed to assess whether the patient is in right- or left-sided CHF, atrial size is the most important piece of information that the clinician can obtain. A patient may have systolic dysfunction or severe LV hypertrophy but still be in a compensated state (i.e. have normal-sized atria), in which case CHF is very unlikely.



6.17 Right parasternal short-axis view at the level of the papillary muscles in a dog with (a) severe tricuspid dysplasia and (b) pulmonic stenosis. (a) There is severe right ventricular eccentric hypertrophy associated with the tricuspid dysplasia. Note the tricuspid valve (arrowed) is visible in the middle of the right ventricle (RV). (b) There is severe right ventricular concentric hypertrophy associated with the pulmonic stenosis. LV = left ventricle.

Pericardium and thoracic cavity assessment: An early diagnosis of pericardial effusion is important because stabilization of these patients may require prompt pericardiocentesis. U-SEE echocardiography is a very helpful test in this respect. Pericardial effusion can be easily detected using the two standard echocardiographic views (i.e. RPLA and RPSA). On both views, fluid (which appears as a hypoechoic region between the epicardium and pericardium) can be seen surrounding the heart (Figure 6.18). It is common to observe a swinging motion of the heart in the pericardial space whenever there is a large volume of effusion present.

Cardiac tamponade is present when the RA and occasionally the RV collapse during diastole (see Figure 6.18). Note that pericardiocentesis is only required if tamponade is present; this is generally the case in dogs, where the pericardial effusion is the main cause of the presenting signs. In contrast, when the volume of pericardial effusion is mild and haemodynamically irrelevant, there is no need to tap the pericardium. This is the more common scenario in cats with CHF.



6.18 Right parasternal (a) long-axis four-chamber view and (b) short-axis view at the level of the papillary muscles in a dog with pericardial effusion. Pericardial effusion (PE) can be easily detected as a hypoechoic/anechoic region around the heart (between the epicardium and pericardium). In (a) note the collapse of the right atrium (RA; arrowed) indicating the presence of cardiac tamponade. LA = left atrium; LV = left ventricle; RV = right ventricle.

The presence of cardiac tamponade in an unstable patient is an indicator for emergency pericardiocentesis. In cases where the patient is stable, a thorough and complete echocardiographic examination should ideally be performed prior to pericardiocentesis to assess for the presence of a mass, as these are most easily seen in the presence of pericardial effusion. However, pericardiocentesis should not be delayed simply to perform a more detailed echocardiographic examination if the patient is severely compromised.

Differentiating between pericardial and pleural effusion is important; the former is typically not seen at the level of the heart base and has smoother, better delineated contours. In cases where both pericardial and pleural effusion are present, the pericardium can be easily delineated as a thin hyperechoic structure encircling the heart.

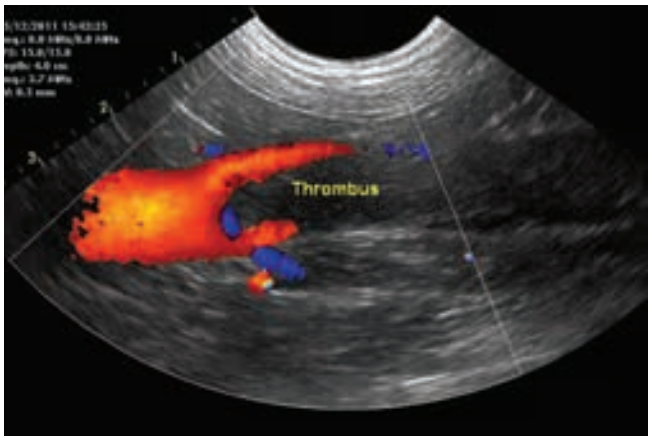
In addition to the standard echocardiographic views described above, the U-SEE examination should include a quick assessment of the thoracic cavity to search for pleural effusion. The ultrasound probe should be advanced cranially and caudally from the point where the echocardiographic images were acquired on both the right and left hemithoraces to look for pleural effusion. In cases where a fluid pocket is identified, this can help guide thoracocentesis. In cats with pleural effusion and a normal-sized LA and RA, the cranial mediastinum should be examined to look for a mass (typically mediastinal lymphoma or thymoma).

Liver and abdominal cavity assessment: The abdominal cavity should be briefly assessed, particularly in cases where hepatomegaly and/or a fluid wave have been detected on physical examination. The liver should be evaluated for size and distension of the hepatic veins. If abdominal effusion (ascites) is present in association with hepatomegaly and a dilated caudal vena cava and hepatic veins, this indicates right-sided CHF. The appearance of the distended hepatic veins is occasionally referred to as the 'bunny sign' (Figure 6.19). Patients in right-sided CHF should have echocardiographic evidence of high RV filling pressures, typically manifested as a markedly dilated RA or pericardial effusion with cardiac tamponade.

In suspected cases of aortic thrombosis, a brief ultrasound examination of the aorta starting at the level of the renal arteries and advancing towards the point of aortic trifurcation can be very rewarding (Figure 6.20). Colour flow and pulsed wave Doppler may be used in these cases to help differentiate between pulsatile blood flow in the aorta and the caudal vena cava.



6.19 U-SEE abdominal ultrasonogram showing hepatomegaly and congested hepatic veins in a dog with right-sided congestive heart failure. The appearance of the distended hepatic veins is sometimes referred to as the 'bunny sign'.



6.20 U-SEE abdominal ultrasonogram of the distal aorta in a dog with paraplegia. A large thrombus is occluding the aorta. Colour flow Doppler shows the absence of blood flow through the aorta.

U-SEE electrocardiography

The ECG part of the U-SEE examination is most important when an arrhythmia or an inappropriately slow or fast heart rhythm has been detected during the physical examination, or when the patient is presented for syncope and weakness. The goal of U-SEE ECG is to look for arrhythmias that could be causing the presenting complaint and/or that require emergency anti-arrhythmic treatment. It is important to remember that not all arrhythmias require treatment and that any antiarrhythmic drug may have a proarrhythmic effect.

As when performing echocardiography, the patient may stand or be gently restrained in sternal or lateral recumbency for U-SEE ECG. A good diagnostic ECG trace can usually be obtained relatively easily without much patient manipulation. The use of atraumatic ECG clips or adhesive ECG patches is very important. In general, dogs tolerate the procedure well in a standing or recumbent position, whereas cats tend to be more cooperative in a sternal or a sitting position. Since the goal of this ECG is the diagnosis of clinically relevant arrhythmias and not to evaluate the size of the different complexes or intervals, the body position of the patient is less important. A continuous 2–5 minute lead II ECG trace is sufficient initially; this simply requires an ECG electrode placed on the right forelimb and another on the left hindlimb.

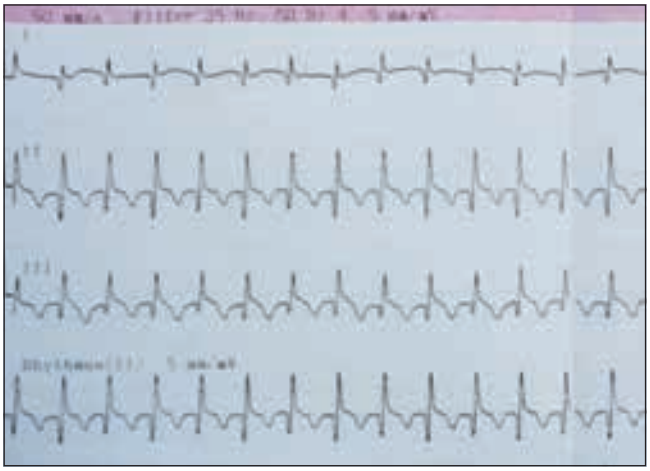
The detection of an arrhythmia alone is neither an indication for antiarrhythmic therapy nor is it necessarily the reason for the presenting complaint. The following factors should be evaluated to determine the clinical relevance of an arrhythmia and to help decide whether therapy is needed:

- A clinically relevant arrhythmia will have haemodynamic consequences, typically resulting in hypotension. Measuring systemic blood pressure and evaluating mental status (e.g. apathy, lethargy, history of syncope) are helpful in this assessment
- As a general rule, the malignant criteria of tachyarrhythmias are as follows:
  - Rapid (paroxysmal or sustained) ventricular tachycardia (>200 beats per minute (bpm))
  - Frequent couplets or triplets of ventricular premature contractions (VPCs)
  - R-on-T phenomenon
  - Sustained or frequent non-sustained bouts of supraventricular tachycardia.

If an arrhythmia is detected, it is very important to interpret this finding together with the information already acquired from the history, physical examination and echocardiogram, which will help determine the relevance and likely cause of the arrhythmia.

The most important arrhythmias in an emergency setting and for which specific treatment will generally be necessary are:

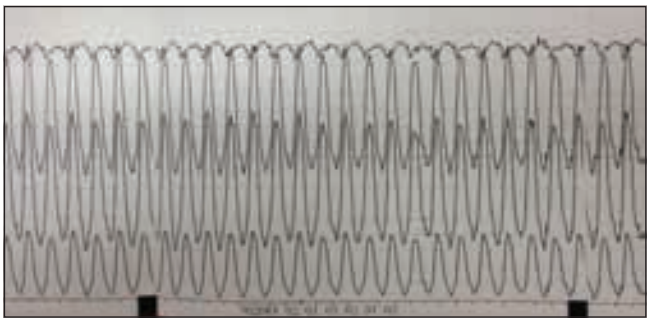
- Sustained or paroxysmal supraventricular tachycardia (Figure 6.21)
- Atrial fibrillation with fast ventricular response rate (Figure 6.22)
- Ventricular tachycardia (Figure 6.23)
- High-grade AV block (second- or third-degree) (Figure 6.24 and 6.40)
- Sick sinus syndrome (Figure 6.25)
- Atrial standstill (Figure 6.26).



6.21 Lead I, II and III ECG recording from an 8-year-old large-breed dog presented with weakness and dyspnoea. There is a fast, regular narrow QRS complex tachycardia (QRS width <70 ms) at 300 bpm. The dog had tachycardia-induced cardiomyopathy and was in left-sided congestive heart failure with pulmonary oedema at initial presentation. Paper speed 50 mm/s; gain 5 mm/mV.



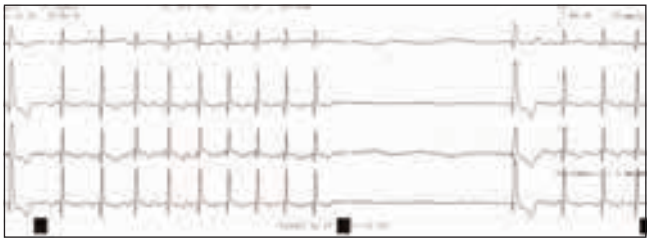
6.22 Lead I, II and III ECG recording from a 7-year-old Boxer with severe subaortic stenosis and congestive heart failure. There is an irregularly irregular narrow QRS complex tachycardia, no P waves and just baseline undulations (f waves). The dog was in atrial fibrillation with a rapid ventricular response rate of 190–270 bpm. Paper speed 50 mm/s; gain 5 mm/mV.



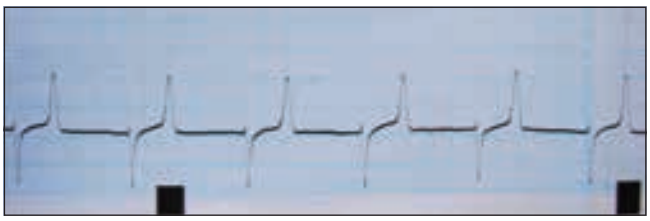
6.23 Lead I, II and III ECG recording from a 6-year-old Boxer with ventricular tachycardia. Note the broad QRS tachycardia (QRS width >70 ms) and very fast rate (500 bpm). This is a life-threatening arrhythmia that requires immediate emergency intervention. Paper speed 50 mm/s; gain 5 mm/mV.



6.24 Lead I, II and III ECG recording from a dog presented for exercise intolerance and syncope. There is complete atrioventricular dissociation with a ventricular escape rhythm at 55 bpm and an atrial rate of 200 bpm. This is diagnostic of a third-degree atrioventricular block. Paper speed 50 mm/s; gain 5 mm/mV.



6.25 Lead I, II and III ECG recording from a West Highland White Terrier presented for collapse. There is a short run of a narrow QRS tachycardia (QRS width <70 ms) (between the second and tenth QRS complexes) at 200 bpm followed by a 1.8 second sinus arrest. The pause is interrupted by a ventricular escape complex and the supraventricular tachycardia restarts. This is an example of tachycardia–bradycardia syndrome or sick sinus syndrome. Paper speed 50 mm/s; gain 5 mm/mV.



6.26 Lead II ECG recording from a cat presented after being hit by a car. There are no P waves or any other atrial activity (flat baseline), the T waves are large and 'tented'. This is a sinoventricular rhythm at 60 bpm. The cat had a bladder rupture and was severely hyperkalaemic, which resulted in atrial standstill. Paper speed 25 mm/s; gain 10 mm/mV.

In canine breeds predisposed to DCM or arrhythmogenic right ventricular cardiomyopathy (ARVC) (i.e. Dobermanns and Boxers, respectively), frequent VPCs (isolated, couplets, triplets) during the 5 minute ECG are relevant. This does not necessarily mean that antiarrhythmic treatment has to be started immediately, but is an indication for continuous ECG telemetry monitoring in the first 24 hours following admission. This approach is also suggested whenever one of these high-risk breeds is presented for syncope, even if the 5 minute ECG recording on presentation shows a normal sinus rhythm, to enable non-sustained but potentially life-threatening arrhythmias to be promptly identified and aggressively treated. Although there are more benign causes of collapse in these breeds (e.g. vasovagal collapse), the significant risk of sudden death in these cardiomyopathic patients warrants careful monitoring.

Summary of the U-SEE examination

1. Place the patient in a sternal or standing position. Administer oxygen simultaneously if indicated and tolerated by the patient.
2. Acquire a RPLA four-chamber and a RPSA (papillary muscle level) view and evaluate the following structures:
   a. LA size in cats – measure the maximal atrial diameter from the interatrial septum to the atrial free wall. Make the measurement parallel to the mitral valve, dissecting the atrium into two equal parts, just prior to mitral valve opening (normal <16 mm) (see Figure 6.11). Typically, the RA is the same size as, or smaller than, the LA
   b. LV – subjective assessment of systolic function (decreased, increased or normal) (see Figure 6.15), concentric *versus* eccentric hypertrophy; in cats, measure LV wall thickness at end-diastole just after the mitral valve closes (normal <6 mm) (see Figure 6.16)
   c. RV – assessment of concentric *versus* eccentric hypertrophy (see Figure 6.17)
   d. Pericardium – evaluate for pericardial effusion and subjectively quantify the volume as mild, moderate or severe; look for RA and/or RV diastolic collapse (cardiac tamponade) (see Figure 6.18).
3. Acquire a RPSA view at the level of the aortic valve and evaluate the following structures:
   a. LA size in dogs and cats – measure the aortic diameter just after aortic valve closure by drawing a line from the middle of the right coronary cusp to the commissure between the non-coronary and left coronary cusps. Extend this line to the LA free wall, avoiding the pulmonary vein entrance, to measure the LA (normal LA/Ao ratio <1.6) (see Figure 6.12)
   b. In cats, use this view to look for 'smoke' and/or a thrombus in the left auricle.
4. Examine both sides of the thorax to look for pleural effusion.
5. Examine the abdomen to look for abdominal effusion, evaluate whether the hepatic veins are enlarged ('bunny sign') (see Figure 6.19) and check for a distal aortic thrombus in cases of acute hindlimb paralysis/paresis (see Figure 6.20).
6. Run a 2–5 minute ECG.

Presumptive diagnosis: decision-making for therapy and stabilization

Once the history and initial stabilization, physical examination and U-SEE examination have been performed, it should be possible to determine whether the presenting complaints are due to a cardiovascular problem and to decide the best approach. The U-SEE flowcharts (see Figures 6.3 to 6.9) indicate the most common differential diagnoses for each of the typical presenting complaints encountered in cardiovascular emergencies.

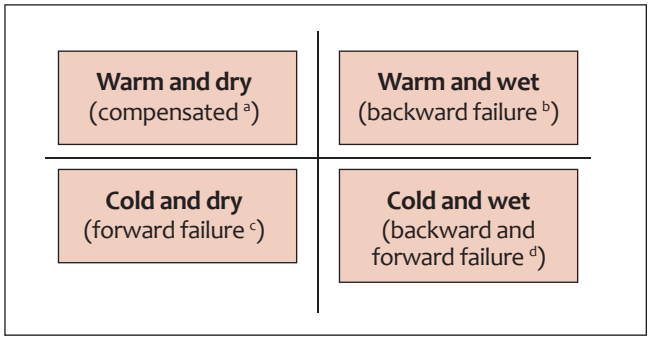
If, during the U-SEE examination, pericardial effusion, pleural effusion or relevant arrhythmias are detected, if signs suggestive of thromboembolism are identified, or if there is a strong suspicion for pulmonary oedema, the appropriate emergency approach should be pursued. These approaches include pericardiocentesis, thoracocentesis, specific antiarrhythmic drugs, anticoagulation/analgesia therapy and diuretic therapy ± inotropic support. The recommended approach for each of these emergency scenarios is presented below.

Acute heart failure

Clinical signs

The clinical signs of heart failure depend on whether the patient is in backward heart failure (congestive), forward heart failure (low cardiac output), or a combination of the two (Figure 6.27).

- Backward heart failure (CHF):
  - Left-sided CHF is characterized by increased respiratory rate and effort. Coughing may occur in dogs and those with severe oedema may cough up blood-tinged fluid. Panting may occur in cats with severe pulmonary oedema
  - Right-sided CHF is characterized by jugular distension, hepatomegaly and ascites
  - Pleural effusion may be seen in cats with either left- or right-sided CHF (left-sided CHF is more common in this species). In dogs, pleural effusion is mainly seen in cases of right-sided CHF (but ascites is typically the main feature of right-sided CHF in this species). The reason for this inter-species difference is not completely clear. In cats, it has been suggested that because the visceral and parietal pleural veins drain into the pulmonary veins and cranial vena cava, respectively, both left- and right-sided heart failure with increased venous pressure may cause pleural effusion. Although pleural drainage in dogs appears to be similar to that in cats, dogs rarely develop pleural effusion secondary to left-sided CHF.
- Forward heart failure (low cardiac output):
  - Low cardiac output failure (cardiogenic shock, (see Chapter 3)) is characterized by weakness, collapse, weak peripheral pulses, pale mucous membranes, hypothermia and cool extremities.



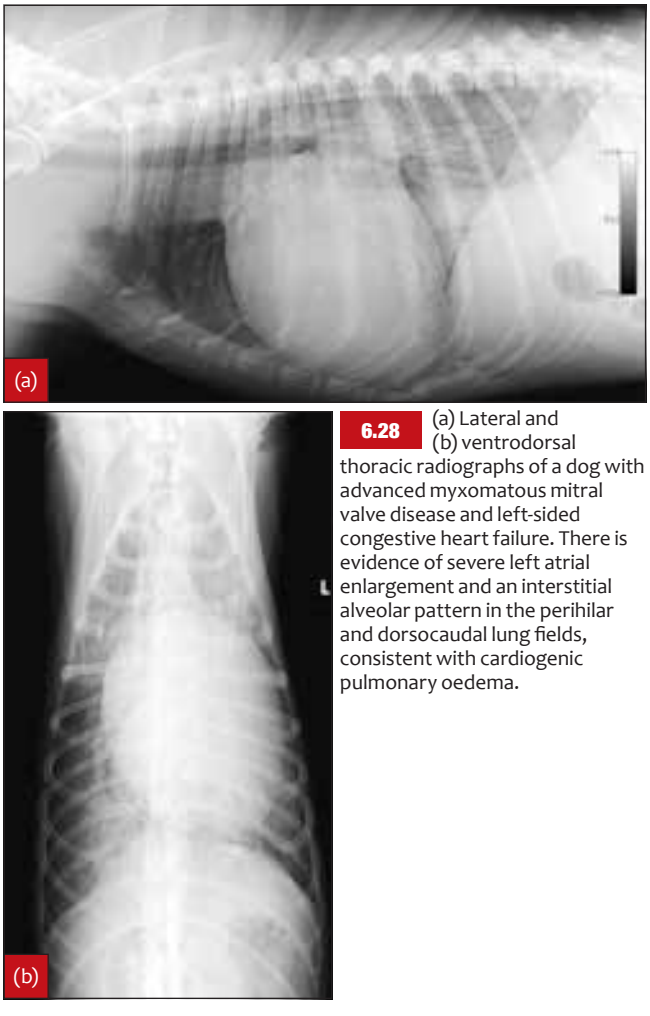
6.27 How heart ('pump') failure manifests clinically. [a]There is evidence of underlying heart disease but no evidence of forward or backward heart failure. [b]There is evidence of pulmonary and/or systemic venous congestion, but cardiac output is maintained. [c]There is evidence of decreased cardiac output, but not of pulmonary and/or systemic venous congestion. [d]There is evidence of decreased cardiac output and pulmonary and/or systemic venous congestion.

Treatment

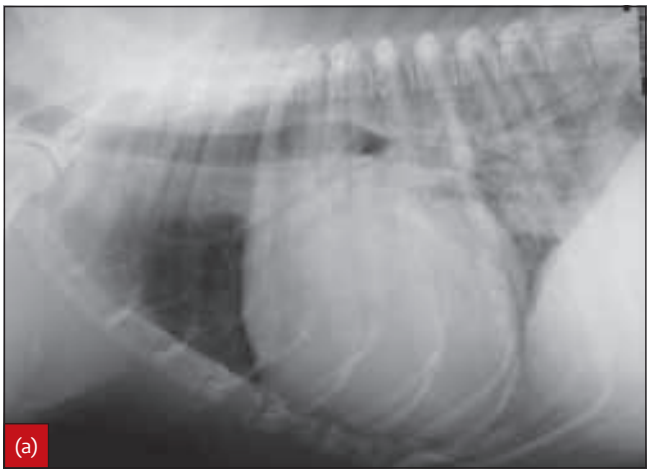
Regardless of the underlying cardiac pathology (e.g. MMVD, DCM, HCM), the principles for treating heart failure are similar. The priorities are clearing fluid accumulations, supporting myocardial function (i.e. attempting to improve systolic or diastolic function or both), decreasing myocardial workload and controlling heart rate and rhythm to optimize cardiac output.

Severe pulmonary oedema (warm and wet)

Pulmonary oedema is the most common cardiac emergency and is typically associated with acute left-sided CHF. Respiratory rate is a very useful indicator of left-sided CHF. Resting respiratory rate should be monitored regularly in the hospital. Thoracic radiography reveals pulmonary oedema or pleural effusion (Figures 6.28 to 6.31) and there is usually echocardiographic evidence of advanced cardiac disease.

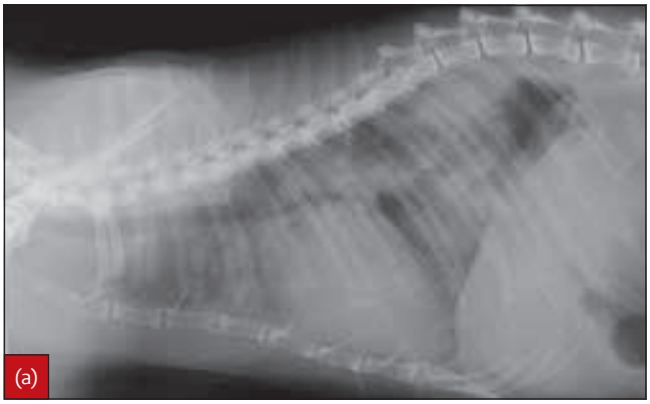


6.28 (a) Lateral and (b) ventrodorsal thoracic radiographs of a dog with advanced myxomatous mitral valve disease and left-sided congestive heart failure. There is evidence of severe left atrial enlargement and an interstitial alveolar pattern in the perihilar and dorsocaudal lung fields, consistent with cardiogenic pulmonary oedema.



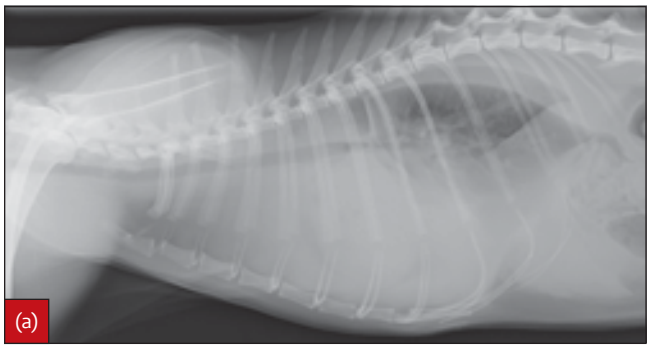


6.29 (a) Lateral and (b) ventrodorsal thoracic radiographs of a dog with advanced dilated cardiomyopathy and left-sided congestive heart failure. There is evidence of left-sided cardiomegaly and an interstitial alveolar pattern in the perihilar and dorsocaudal lung fields, consistent with cardiogenic pulmonary oedema.





6.30 (a) Lateral and (b) ventrodorsal thoracic radiographs of a cat with advanced cardiomyopathy and left-sided congestive heart failure. There is evidence of cardiomegaly and a diffuse alveolar pulmonary pattern consistent with pulmonary oedema. In cats, cardiogenic pulmonary oedema often does not show a typical caudodorsal distribution pattern, as it does in dogs. The pulmonary pattern associated with pulmonary oedema in cats may have any type of distribution (i.e. focal, diffuse or multifocal interstitial to alveolar pattern).





6.31 (a) Lateral and (b) dorsoventral thoracic radiographs of a cat with pleural effusion, which is obscuring the cardiac silhouette.

Dogs and cats with left-sided CHF (pulmonary oedema in dogs; pulmonary oedema and/or pleural effusion in cats) can be very unstable. Stress can cause further cardiac decompensation and the patient may be too unstable to safely take a radiograph at presentation to confirm the diagnosis of pulmonary oedema or pleural effusion. A quick U-SEE examination should be performed, if possible, to assess LA size, which will help confirm the likelihood of pulmonary oedema. The thorax should also be checked for the presence of pleural effusion (see Figure 6.7). If there is a high suspicion for pulmonary oedema, the patient should be treated presumptively with diuretics. The response to treatment should be assessed by monitoring for a decrease in respiratory rate. Pulmonary oedema almost always responds to furosemide, as long as the dose is sufficient. A moderate to large volume of pleural effusion will need to be drained at presentation, as this will not reduce significantly with diuretic therapy alone.

Summary of acute stabilization of CHF

The recommendations for acute stabilization (ACVIM Consensus Statement 2009) include:

- Hospitalization for cage rest and close monitoring (in a quiet, minimum stress environment where possible)
- Oxygen therapy
- Opioid sedation if the patient is very anxious
- Furosemide (intravenously or intramuscularly)
- Consideration of whether to administer vasodilators ± positive inotropes
- Thoracocentesis and abdominocentesis as required.

Oxygen therapy: The method for administering oxygen therapy depends on practicality and which is tolerated best by the patient. Arterial blood gas analysis, if available, can be used to evaluate hypoxia. Any level of hypoxia warrants at least temporary oxygen supplementation. A partial pressure of oxygen (P_aO_2) of <60 mmHg or oxygen saturation of <90% is an indication for aggressive oxygen therapy.

- Mechanical ventilation or non-invasive positive pressure ventilation (CPAP) is a consideration (if practical) for patients with progressive respiratory fatigue, lack of P_aO_2 response to oxygen supplementation or progressive hypercapnia.
- Oxygen cages provide 40–90% inspired oxygen in a humidified and temperature controlled environment. Care must be taken to avoid overheating, especially in large or panting patients.
- Intranasal oxygen is provided at a flow rate of 0.5–1 l/minute. If administered for more than a few hours, oxygen should be humidified and an Elizabethan collar used to prevent the patient from removing the nasal catheter.
- Other ways of administering oxygen include facemasks or the use of an Elizabethan collar and cellophane to make an 'oxygen hood'. Oxygen flow rates of 5–10 l/minute are used and the oxygen should be humidified.

Diuretics: These are used to control oedema formation; oedema in CHF is due to increased circulating blood volume. Total circulating blood volume can be increased by as much as 30% in severe CHF due to chronic activation of the renin–angiotensin–aldosterone system (RAAS) and resultant fluid retention.

Important considerations when using diuretics include the possible development of azotaemia or electrolyte imbalances. Renal function should be monitored closely for 24–48 hours after initiation or a dose increase. Some degree of azotaemia may be unavoidable in patients with advanced heart disease and compromised cardiac output. Increasing the frequency of diuretic dosing should be considered to spread the diuretic effect, rather than increasing the overall dose. It is important to monitor serum potassium levels regularly, particularly in inappetent, dehydrated patients when high diuretic doses are used.

Furosemide: This drug is the most important diuretic for treatment of acute CHF. It acts in the thick portion of the ascending loop of Henle and has a rapid onset of action (following intravenous administration an effect is seen within 5 minutes). The dosage range is very wide and initial intravenous boluses can be followed by a constant rate infusion (CRI) if necessary (Figure 6.32).

The severity of the dyspnoea and improvement in the respiratory rate should be monitored as a guide to treatment success. It is also important to monitor renal parameters and electrolytes, especially potassium. Furosemide also has some bronchodilation properties when given intravenously and a mild antitussive action via affecting laryngeal nerve sensitivity. This explains why some dogs incorrectly treated with furosemide stop coughing even though they are not in CHF.

A furosemide CRI can be effective in dogs (and cats) with severe left-sided CHF that have a poor response to boluses. Studies in humans (healthy patients and those with CHF) and healthy dogs and horses suggest that compared with intravenous boluses, a furosemide CRI results in increased diuresis, decreased volatility in plasma volume, increased natriuresis and calciuresis, decreased kaliuresis and, possibly, decreased activation of the RAAS.

Positive inotropes: These drugs have beneficial haemodynamic effects in patients with systolic heart failure due primarily to a direct increase in myocardial contractility and therefore cardiac output. By increasing the force of myocardial contraction, it is easier for the failing LV to eject blood into the circulation. These drugs are not indicated in cases where augmentation of cardiac output via increased contractility is not possible (e.g. fixed aortic stenosis). Positive inotropes are in general not indicated in cats with HCM and their use in HCM is reserved for patients with systolic dysfunction (i.e. end-stage HCM), but this is an off-label use. Until further studies are undertaken obstructive HCM (HOCM) should be considered as a contraindication to the use of positive inotropes.

Pimobendan: This is a calcium-sensitizing drug which acts as a positive inotrope to improve contractility. It is a phosphodiesterase III inhibitor that also decreases cardiac afterload by causing arterial vasodilation, thereby making it easier for the heart to pump blood into the circulation. This is why pimobendan is referred to as an inodilator. Pimobendan is available in oral and intravenous formulations. It has a slower onset of action if given orally (within several hours). It should be remembered that oral medications will not be absorbed from the gut reliably in patients with heart failure and impaired circulation. In addition, it may be stressful to the patient to administer oral medication.

Dobutamine: This drug is a selective beta-1 adrenergic agonist. It increases contractility with a minimal increase in heart rate and blood pressure. It must be administered via CRI using a syringe or fluid infusion pump and titrated to effect (see Figure 6.32). It has a short half-life and thus a rapid onset and offset of action. There is a risk of supraventricular or ventricular tacharrhythmias with higher doses. Dogs being treated with dobutamine should have their blood pressure measured regularly and should be continuously monitored using electrocardiography. Tolerance to the inotropic effects of dobutamine occurs with prolonged infusion.

Dopamine: This drug has similar effects to those of dobutamine, except at high doses dopamine causes vasoconstriction (and increased systemic vascular resistance) through alpha-adrenergic receptor agonism. Dopamine may be slightly more proarrhythmic than dobutamine, therefore the dose should be kept as low as possible to achieve the desired aim.

Vasodilators: These drugs, in particular arterial dilators, allow rapid 'unloading' of the ventricle. They are indicated in patients with severe pulmonary oedema due to impaired LV systolic function or mitral insufficiency. By decreasing systemic vascular resistance, it is easier for the failing LV to eject blood into the circulation. In patients with significant mitral regurgitation, the regurgitant fraction is decreased, thus lowering LA pressure.

In order to obtain this response, the LV must be able to sustain an adequate stroke volume. Thus, potent arterial vasodilation is contraindicated in animals with a fixed LV stroke volume (e.g. HCM, mitral stenosis, aortic stenosis). This also applies to severely hypovolaemic patients, which must first be volume resuscitated. Severe pulmonary oedema in animals with a fixed LV stroke volume must be managed primarily by preload reduction (e.g. furosemide, venodilators).

Clinical signs of effective arterial vasodilation include bright pink mucous membranes with a rapid capillary refill time, warm extremities and a gradual decrease in

Drug	Dosage
Diuretics	
Furosemide	Dogs: 2–6 mg/kg i.v., i.m., s.c. q6–12h or orally q8–24h Cats: 1–4 mg/kg i.v., i.m., s.c., orally q12–48h CRI: 0.5–1.0 mg/kg/h i.v. for a maximum of 6 hours
Inotropes	
Dobutamine	Dogs: 2–15 µg/kg/min i.v.; start CRI low and titrate to effect Cats: 1–5 µg/kg/min i.v.; start CRI low and titrate to effect
Dopamine	Dogs: 2–10 µg/kg/min Cats: 1–5 µg/kg/min i.v.; start CRI low and titrate to effect
Pimobendan	Dogs, cats: 0.15 mg/kg i.v. q12h or 0.1–0.3 mg/kg orally q12h (target dose of 0.25–0.3 mg/kg orally q12h recommended in dogs)
Vasodilators	
Amlodipine	Dogs: 0.05–0.1 mg/kg orally q12–24h Cats: 0.625–1.25 mg/cat orally q24h
Hydralazine	Dogs: 0.5–3 mg/kg orally q12h
Sodium nitroprusside	Dogs, cats: 0.5–10 µg/kg/min i.v.; start CRI low and titrate to effect while monitoring blood pressure closely
Antiarrhythmics	
Amiodarone	Dogs: 10–15 mg/kg orally q12h for 7 days, then 5–7.5 mg/kg orally q12h for 14 days, then 7.5 mg/kg orally q24h Nexterone (injectable amiodarone without polysorbate 80 and benzyl alcohol): 2 mg/kg i.v. bolus over 10 minutes followed by CRI at 0.8 mg/kg/h for 6 hours, then CRI at 0.5 mg/kg/h
Atenolol	Dogs: 0.5–2 mg/kg orally q12h; start low and titrate to effect Cats: 6.25–12.5 mg/cat total dose orally q12–24h
Digoxin	Dogs: 0.003–0.005 mg/kg q12h. Avoid in cats, as they are more sensitive to the toxic effects of digoxin than dogs
Diltiazem	Dogs, cats: 0.05–0.25 mg/kg i.v. (over 1–2 minutes), CRI at 3–6 µg/kg/min; 0.5–2 mg/kg orally q8h or 1 x 10 mg tablet for cats q8h Dogs (extended-release preparation): 3 mg/kg orally q12h
Esmolol	Dogs, cats: 0.05–0.5 mg/kg i.v. bolus over 5 minutes; CRI at 25–200 µg/kg/min
Lidocaine	Dogs: 2–8 mg/kg i.v. given in 2 mg/kg boluses followed by CRI at 30–80 µg/kg/min Cats: 0.2–0.4 mg/kg i.v. slow bolus
Magnesium	0.1–0.2 mmol/kg slow i.v. (over 5–10 minutes) followed by CRI at 0.5–1.0 mmol/kg/day
Mexiletine	Dogs: 4–8 mg/kg orally q8–12h
Procainamide	Dogs: 6–8 mg/kg i.v. (over 5 minutes), i.m. q6h or CRI at 0.025–0.05 mg/kg/min
Propranolol	Dogs: 0.1–1.5 mg/kg orally q8h Cats: 2.5–5 mg total dose orally q8h; start low and titrate to effect
Sotalol	Dogs: 0.5–2 mg/kg orally q12h (start low and titrate to effect) or 1 mg/kg i.v. over 3–5 minutes Cats: 10–20 mg/cat orally q12h
Analgesics	
Buprenorphine	Dogs, cats: 0.02–0.03 mg/kg i.v., i.m. q6h
Fentanyl	Dogs, cats: 2–5 µg/kg slow i.v. followed by CRI at 2–5 µg/kg/h
Methadone	Dogs, cats: 0.2–0.4 mg/kg slow i.v., i.m. q4–6h
Antithrombotics	
Aspirin	Dogs: 0.5 mg/kg orally q24h Cats: 18.75 mg orally q72h (¼ of a 75 mg tablet)
Clopidogrel	Dogs: 1–3 mg/kg orally q24h Cats: 18.75 mg/cat orally q24h (¼ of a 75 mg tablet)
Dalteparin (low molecular weight heparin)	Dogs, cats: 100–200 IU/kg s.c. q12–24h
Enoxaparin (low molecular weight heparin)	Dogs, cats: 1–2 mg/kg s.c. q12–24h
Unfractionated heparin (anticoagulation)	Dogs, cats: 200–300 IU/kg i.v. initially, then 250–300 IU/kg s.c. q8h
Other	
Atropine	Dogs, cats: atropine response test – 0.04 mg/kg i.v., s.c.
Calcium gluconate	Dogs, cats: 0.5–1.5 ml/kg of a 10% solution slowly i.v. for the treatment of hyperkalaemia
Dextrose	Dogs, cats: 0.5–1.5 mg/kg 50% dextrose i.v. for the treatment of hyperkalaemia; may be administered with insulin
Insulin	Dogs, cats: 0.5–1.0 IU/kg i.m. plus 2 g dextrose i.v. per unit of insulin

6.32 Drugs used for the treatment of cardiovascular emergency patients. Ranges are approximate and clinical evaluation of the patient dictates dosage of drugs to be administered. CRI = constant rate infusion.

respiratory rate and effort. Clinical signs of hypotension include weakness, collapse, tachycardia and worsening renal biochemistry values.

Sodium nitroprusside: This drug is a rapid-acting and potent 'mixed' vasodilator, resulting in both preload and afterload reduction. It is mandatory to administer nitroprusside via CRI using a syringe or fluid infusion pump, as this drug is extremely potent and the dose must be accurately controlled (see Figure 6.32). It has a rapid onset and offset of action, with a half-life of minutes, and should be titrated to effect. Close blood pressure monitoring is required with the use of nitroprusside. Direct arterial blood pressure monitoring is the most accurate method, although Doppler or oscillometric non-invasive methods can also be used. Target mean arterial blood pressure should be approximately 70–80 mmHg. Nitroprusside can be used to effectively reduce arterial pressure and is especially indicated for the treatment of animals in acute severe CHF.

Known hypotension is a contraindication for the administration of nitroprusside, but normal arterial blood pressure accompanying low cardiac output and CHF signs is an indication for its use. The drug is light-sensitive and should be prepared in relatively high concentrations, allowing low fluid administration rates compatible with CHF. Any additional fluid therapy or drug infusions should be given separately to allow independent changes in administration rate. After 48–72 hours of CRI, there is an increased risk of toxicity (cyanide). Rapid improvement in the clinical signs is usually noted in the first 3–6 hours when nitroprusside is administered concurrently with furosemide and other adjunctive therapies.

Pimobendan: This drug is a balanced vasodilator; see above for further information.

Angiotensin-converting enzyme inhibitors: These drugs are important in the treatment of chronic CHF but are less helpful in cases of acute pulmonary oedema due to their slower onset of action and relatively mild arterial dilation compared with other more potent vasodilators. These drugs are for oral administration only.

Hydralazine: This drug is a potent oral arterial dilator that can be used to treat both acute and chronic heart failure. Indications for use in acute pulmonary oedema are the same as those for sodium nitroprusside. Hydralazine may be chosen for acute therapy if sodium nitroprusside is not readily available or financial constraints preclude the use of a CRI.

Contraindications for the use of hydralazine are similar to those for sodium nitroprusside. An arterial blood pressure measurement should be obtained prior to therapy to exclude hypotension. Animals with fulminant pulmonary oedema are usually given a higher initial dose of hydralazine than patients with more chronic signs or animals already receiving chronic vasodilator therapy.

Blood pressure should be assessed approximately 1 hour after dosing. The target response is a mean or systolic (if measured by Doppler sphygmomanometry or oscillometry) arterial blood pressure decrease of up to 20 mmHg, as long as the systolic arterial pressure remains >90 mmHg and the mean arterial pressure remains >60 mmHg. When an effective dose has been documented, that dose should be repeated at 12-hour intervals.

Amlodipine: This drug is a second-generation calcium channel blocker that acts as an arterial dilator by inhibiting calcium influx into the arterial vascular cells. Indications and contraindications for use are similar to those of hydralazine. This drug is for oral administration only.

Severe low-output failure and cardiogenic shock (dry and cold)

Low-output cardiac failure is a challenging emergency presentation. Certain serious cardiac arrhythmias can lead to clinical signs of low-output failure, so an ECG is mandatory in these patients. Low cardiac output can be exacerbated by hypovolaemia in patients with cardiac disease, and is usually the result of complications of CHF therapy (e.g. over-diuresis).

The initial assessment of the hypovolaemic patient with low-output cardiac failure should include serum biochemical analysis to document organ dysfunction and any electrolyte imbalances. The therapeutic plan includes cautious intravenous rehydration. Any electrolyte disturbances or drug toxicities must be addressed, whilst administering positive inotropic medications to improve cardiac output. Fluids should be supplemented with potassium and magnesium based on measured blood electrolyte concentrations of these electrolytes. In most cases, maintenance fluid administration rates (2 ml/kg/h) are sufficient for initial supplementation, and the use of fluid pumps for accurate control of fluid volume administration is highly recommended.

Most patients with clinical signs of hypovolaemia and no current evidence of CHF will benefit from the reduction or temporary discontinuation of diuretic therapy. Discontinuation of vasodilators must be approached with more caution, as rebound hypertension may occur if vasodilators are discontinued abruptly. Positive inotropic drugs should be administered to increase cardiac output, once rehydration has been instigated. Respiratory rate and effort must be monitored closely during rehydration as CHF secondary to fluid overload may develop suddenly. Success of fluid therapy is monitored through physical examination, bodyweight, arterial blood pressure, urine output and blood tests.

Low cardiac output with pulmonary oedema (cold and wet)

This clinical presentation may occur with severe systolic or severe diastolic dysfunction.

Severe systolic dysfunction: This is typical of dogs and cats with DCM. Decreased systolic function is accompanied by increased filling pressures, but cardiac output is still inadequate. These patients present with clinical weakness, collapse or signs of shock accompanied by pulmonary oedema, with or without arrhythmias. They are most often normotensive or mildly hypotensive, with systolic arterial blood pressure in the range of 80–90 mmHg, but have poor perfusion with cold extremities due to peripheral vasoconstriction.

The combination of arterial dilators and positive inotropes often increases cardiac output enough to decrease LA pressure and relieve pulmonary oedema, making the administration of high doses of furosemide unnecessary. If the oedema does not resolve rapidly enough, low to moderate doses of furosemide may be used to decrease preload. Rapid, aggressive diuresis should be avoided unless the oedema is life-threatening, because it is important to avoid hypovolaemia/dehydration, which might result in worsening of low-output signs.

Severe diastolic dysfunction: This is most commonly seen in cats with HCM or RCM. Acute low cardiac output due to diastolic dysfunction is usually accompanied by pulmonary oedema. In diseases typified by diastolic dysfunction, systolic function is usually normal or increased. Relief of pulmonary oedema is achieved by the administration of diuretics and venodilators (see above), but care must be taken to avoid over diuresis and arterial hypotension. Arterial vasodilation is contraindicated in acute heart failure caused by diastolic dysfunction.

In severe cases, dobutamine infusions may be indicated to increase cardiac output and relieve oedema. Although dobutamine is usually referred to as a positive inotrope, it also has powerful lusitropic (promotes ventricular relaxation) effects. Administration of a dobutamine CRI to cats with severe pulmonary oedema, together with cautious diuretic therapy, can lead to rapid resolution of the pulmonary oedema without induction of severe dehydration. Pimobendan may be useful as well in such cases, although this is currently an off-label use in cats.

In cats that have sinus or other supraventricular tachycardias, administration of a calcium channel blocking agent (such as diltiazem) may improve diastolic function by slowing heart rate. Once the pulmonary oedema has resolved, beta-blocking agents can be used instead of calcium channel blockers to slow the heart rate if preferred. However, the use of beta-blockers is contraindicated if CHF is present, or if calcium channel blockers or dobutamine are already being used.

Pericardial effusion

Key points

- Typical clinical signs/physical examination findings: weakness, syncope, distended jugular veins, weak femoral pulses, tachycardia, muffled heart sounds and ascites. Patients with acute cardiac tamponade may present in cardiogenic shock.
- Diagnosis: echocardiography is the most sensitive and specific test for diagnosing and assessing the clinical relevance of a pericardial effusion.
- Treatment: pericardiocentesis is the treatment of choice for pericardial decompression and should be performed as an emergency procedure whenever there is evidence of cardiac tamponade (RA or RV collapse identified on echocardiography). In cats, pericardiocentesis is generally not necessary because cardiac tamponade is rare.
- Prognosis: The prognosis for dogs with pericardial effusion is quite variable; it may be good to excellent in cases of idiopathic pericarditis, fair in cases of heart base tumours (chemodectomas) or mesotheliomas, and poor in cases of haemangiosarcoma. In cats with pericardial effusion secondary to CHF and advanced cardiac disease, the prognosis is typically poor.

The pericardium is a fibrous sac surrounding the heart and has three main functions:

- It anchors the heart in position within the thorax
- It provides external support for the heart, which prevents excessive cardiac chamber dilatation
- It prevents extension of infection or inflammatory processes to the myocardium from other structures within the thoracic cavity.

Typically, the pericardium is thin and minimally distensible and filled with a low volume of fluid (0.25 ml/kg). Pericardial effusion refers to an excessive accumulation of pericardial fluid and is the most frequently acquired pericardial disease in dogs and cats. Cardiac tamponade occurs whenever the accumulation of fluid within the pericardium compresses the cardiac chambers and prevents adequate cardiac filling. As the right side of the heart is relatively thin-walled and operates at low pressures, it is preferentially affected in comparison with the left side of the heart. Increased pericardial fluid results in restriction of RA filling, diastolic RA collapse and subsequently diastolic RV collapse. Signs of right-sided CHF predominate.

Cardiac tamponade may occur with small- or large-volume effusions, depending on how quickly the pericardial fluid accumulates. Large pericardial effusions suggest a more chronic process in which the pericardium has had sufficient time to distend, whilst small amounts of pericardial fluid suggest a more acute process with rapid accumulation of fluid (e.g. following intrapericardial bleeding from a neoplasm or atrial rupture). Patients are typically tachycardic to maintain cardiac output in the face of reduced stroke volume.

Cardiac tamponade is more frequently encountered in dogs and is rare in cats. Rarely, a minimal effusion may result in significant tamponade if constrictive pericarditis (constrictive–effusive) is present. In this situation, the pericardium is very stiff, thick and fibrotic, and minimal fluid accumulation will cause severe intrapericardial pressure elevation and significant haemodynamic compromise. Diagnosis can be difficult in these cases.

During a normal respiratory cycle, inspiration reduces intrathoracic pressure and improves venous return to the heart and right-sided filling. In the presence of cardiac tamponade, the increased systemic venous return expands the right side of the heart and directly compromises filling of the left side, with subsequent decreased cardiac output. The fall in arterial pressure that occurs during inspiration is called pulsus paradoxus.

History

Patients that develop pericardial effusion acutely (within the previous 24 hours) are usually suddenly unwell, weak, lethargic and unable to stand or walk. Chronic cases where the pericardial effusion has developed over several days to weeks often have a history of gradual progression of weakness, exercise intolerance, abdominal distension (hepatomegaly, ascites), marked recent weight gain (3–5 kg) and sometimes exertional syncope. Polydipsia is frequently described in the 24–48 hours before presentation in cardiac tamponade. This is likely to be due to activation of neurohormonal compensatory mechanisms as cardiac output falls.

Clinical signs and physical examination

Acute cases that present in obstructive shock are often in lateral recumbency or severely weak with pale or cyanotic mucous membranes, tachycardia, muffled heart sounds, weak femoral pulses and cold peripheral extremities. Ascites is usually not present or is just mild.

Chronic cases usually have tachycardia, weak femoral pulses or occasionally pulsus paradoxus, muffled heart

sounds, jugular vein distension or positive hepatojugular reflux (distended jugular veins once sustained pressure is applied to the abdomen), hepatomegaly, ascites and/or pleural effusion (dyspnoea/tachypnoea, ventrally muffled lung sounds). In large pericardial effusions, there may be a direct compressive effect of the enlarged heart causing tachypnoea or coughing.

A constellation of signs termed 'Beck's triad' (weak arterial pulses, distended jugular veins and muffled heart sounds) is considered almost pathognomonic for pericardial effusion. Occasionally, pericardial effusion can present with non-specific clinical signs. Patients are vaguely unwell and may present with lethargy, reduced appetite, abdominal pain, weight loss, vomiting or cough, thereby making the diagnosis challenging. Thus, the differential diagnoses of pericardial effusion and cardiac tamponade should be borne in mind for dogs presenting with tachycardia or relative tachycardia and vague signs.

Diagnosis

U-SEE examination

Echocardiography: This is the most sensitive and specific test for pericardial effusion. U-SEE ECHO should be performed immediately in any case presented in cardiogenic or obstructive shock, so that pericardial effusion can be rapidly diagnosed and an appropriate stabilization approach initiated (intravenous fluids, pericardiocentesis). It should also be performed in any case presented with ambiguous clinical signs, weakness and tachycardia.

In stable patients, a more thorough (complete) echocardiographic examination is desirable as it is easier to identify masses when there is pericardial effusion surrounding the heart, as it creates a better acoustic window (better contrast). Ideally, an experienced echocardiographer should perform such an examination, but if this is not possible, U-SEE ECHO (see Figures 6.3, 6.7 and 6.8) and emergency pericardiocentesis should be performed. Echocardiography has been shown to be highly specific (100%) and sensitive (82%) for the detection of cardiac masses, as well as having high positive (100%) and negative (75%) predictive values (MacDonald *et al*., 2009).

In RPLA and RPSA views, pericardial effusion appears as a hypoechoic or anechoic area around the heart (see Figure 6.18). In cases of large-volume effusions, a swinging motion of the heart in the pericardial space is seen. Cardiac tamponade is present when there is RA inversion/collapse; occasionally, this collapse can also be observed involving the RV free wall. It is typically seen transiently in diastole but may persist throughout the cardiac cycle in more severe cases.

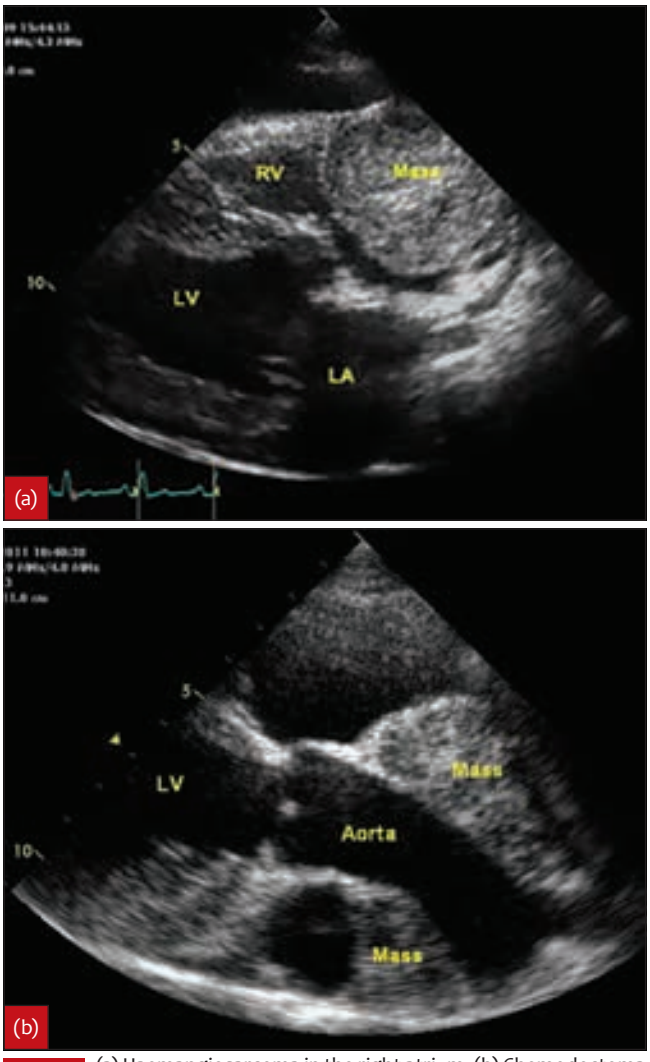
PRACTICAL TIP

RA collapse is best seen on the RPLA view, while RV free wall inversion is better evaluated on the RPSA view (at the level of the heart base or papillary muscles)

Echocardiographic evaluation for cardiac tamponade is mandatory because in these cases pericardial effusion is haemodynamically relevant and pericardiocentesis should be performed urgently:

- The cardiac chambers are usually small and underfilled due to the high intrapericardial pressure and reduced preload. As a result, the ventricular walls may appear thicker than normal (pseudohypertrophy)
- Masses are most frequently detected in/on the right auricle, suggestive of a haemangiosarcoma (Figure 6.33a), or at the heart base (around the aorta), suggestive of a heart base tumour (most commonly chemodectomas) (Figure 6.33b). The differentiation between RA and heart base masses is very important because the latter are typically associated with a much better prognosis and pericardectomy may improve survival
- In addition to the typical location in the RA, haemangiosarcomas often have a cystic appearance with small hypoechoic foci, whilst heart base tumours have a more homogeneous echogenicity.

It is also worth considering evaluation of the spleen for a primary mass or metastases. The presence of a splenic mass and pericardial effusion is suggestive of haemangiosarcoma and is helpful in prognostication. In one study, 29% of dogs with RA haemangiosarcoma had concurrent splenic haemangiosarcoma (Boston *et al*., 2011). However, as there are other more benign and incidental causes for splenic masses, patients should be stabilized by pericardiocentesis until further diagnostic tests and evaluation are performed.



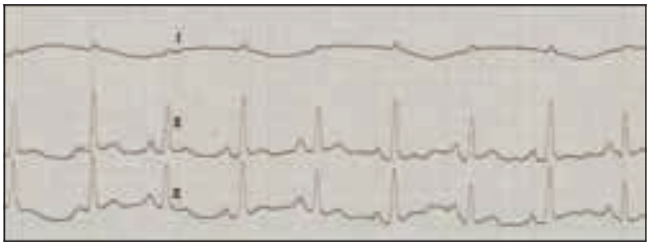
6.33 (a) Haemangiosarcoma in the right atrium. (b) Chemodectoma encirling the aorta (heart base tumour). These are the two most commonly detected cardiac masses. Differentiation between the two types of neoplasm is important because they are associated with different prognoses. LA = left atrium; LV = left ventricle; RV = right ventricle.

In cats, LV wall thickness and LA size should be assessed on a RPLA and/or RPSA view. CHF is the most common cause of pericardial effusion in this species and HCM is the most frequently diagnosed feline cardiomyopathy.

Pitfalls in U-SEE ECHO

- A severely enlarged LA and pleural effusion can sometimes be confused with pericardial effusion.
- Non-neoplastic causes of mass effects: these include enlarged atria and auricular appendage, papillary muscles or attachments, hyperechoic foci in the AV groove (RA to RV transition) and heart base – typically fat, thrombus in the pericardial sac in cases of atrial tears, consolidated or collapsed lung lobe and fibrin tags.

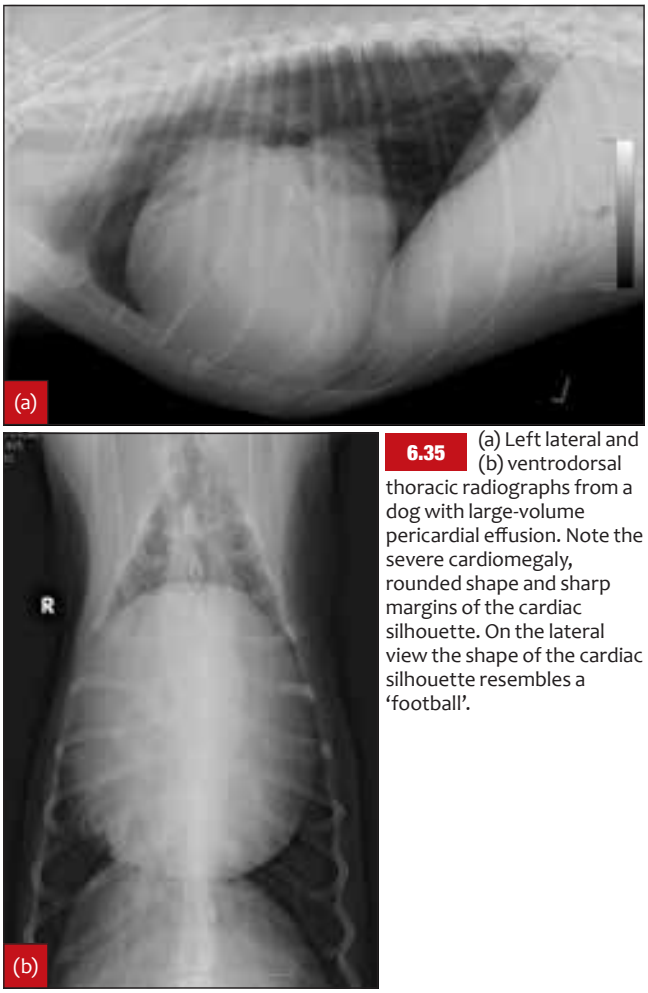
Electrocardiography: This is an insensitive test for pericardial effusion. Sinus tachycardia is the most frequent rhythm observed. More specific findings for pericardial effusion are low-voltage QRS complexes (<1 mV) and electrical alternans, which represents an alternating variation in the height of the QRS complexes, postulated to reflect swinging of the heart within the fluid-filled pericardium (Figure 6.34). Supraventricular and ventricular arrhythmias (isolated VPCs are more frequent than ventricular tachycardia) may be observed. It is important to differentiate ventricular tachycardia from an accelerated idioventricular rhythm (ventricular rate <160 bpm), which is often a benign arrhythmia that can be seen in cases of severe systemic disease (commonly seen in animals with splenic masses) (see Figure 6.46).



6.34 Lead I, II and III ECG recording from a 9-year-old German Shepherd Dog with severe pericardial effusion showing electrical alternans. Note the variation in height of QRS complexes with alternating beats. Paper speed 50 mm/s; gain 5 mm/mV.
(Courtesy of Dr T Glaus)

Radiography

Radiography is generally insensitive in cases of low-volume pericardial effusions. In patients with large effusions, the cardiac silhouette is round with sharply defined borders (sometimes described as a 'football' or 'pumpkin' shaped cardiac silhouette) and there is increased diaphragmatic overlap and tracheal elevation (Figure 6.35). In cases of cardiac tamponade and right-sided CHF, a distended caudal vena cava, hepatomegaly, abdominal effusion (loss of abdominal detail) and pleural effusion may be present. The radiograph should also be evaluated for the presence of a heart base mass, which is seen as a soft tissue opacity over the heart and displacement of the trachea (dorsally on lateral views and laterally on dorsoventral/ventrodorsal views). Metastases should be checked for, although thoracic radiographs may have a low sensitivity for the detection of pulmonary metastases compared with computed tomography (CT).



6.35 (a) Left lateral and (b) ventrodorsal thoracic radiographs from a dog with large-volume pericardial effusion. Note the severe cardiomegaly, rounded shape and sharp margins of the cardiac silhouette. On the lateral view the shape of the cardiac silhouette resembles a 'football'.

Blood pressure

Hypotension is observed in severe cardiac tamponade and obstructive cardiogenic shock. A systolic blood pressure <90 mmHg or mean blood pressure <60 mmHg reflects severe haemodynamic compromise and a life-threatening condition that should prompt immediate pericardiocentesis.

Clinical pathology

Several haematological and blood chemistry changes may be observed with pericardial effusion, although they lack specificity.

- Anaemia, if present, is typically mild, normocytic, normochromic and non-regenerative. Morphological red blood cell abnormalities, such as schistocytes or acanthocytes, may be seen with haemangiosarcoma, although they are not regularly present.
- Thrombocytopenia can occur due to consumption of platelets.
- Increased liver enzymes (mild to moderate increase).
- A coagulation profile should be performed in cases where there is a suspicion that a coagulopathy and spontaneous bleeding may be the cause of the pericardial effusion. This may reveal clinical or subclinical evidence of a coagulopathy.
- Cardiac troponin I may be useful in discriminating between different causes of pericardial effusion (mainly cardiac haemangiosarcoma). A cut-off of >0.25 ng/ml has been suggested to detect cardiac

haemangiosarcoma in dogs with pericardial effusion, with a sensitivity of 81% and specificity of 100% (Chun *et al*., 2010). However, inconsistent results are found in the literature.
- Peritoneal effusion is typically a modified transudate.
- Pericardial fluid analysis in dogs usually classifies it as haemorrhagic fluid. Neoplasia is difficult to diagnose from pericardial fluid samples since haemangiosarcoma and mesothelioma exfoliate poorly and neoplastic mesothelial cells may be hard to distinguish from reactive mesothelial cells. An exception is cardiac lymphoma, which is more exfoliative and cytology may be diagnostic. Infectious causes of pericardial effusion are rare but can occur secondary to penetrating wounds and migrating foreign bodies, particularly grass seeds. Cytology may be useful to exclude an infectious aetiology and culture is sensible if an infectious cause is suspected.

Pericardial effusions in dogs

The most common causes of pericardial effusion in dogs are cardiac neoplasia and idiopathic pericarditis (Figure 6.36). The most frequently affected breeds are Golden Retrievers, Labrador Retrievers and German Shepherd Dogs.

Cardiac neoplasia

Two tumour types are by far the most commonly diagnosed: haemangiosarcoma and chemodectoma. Staging of suspected tumours is rarely performed, although CT and magnetic resonance imaging (MRI) for surgical planning and metastasis screening is possible. Referral to an oncologist should always be considered.

Haemangiosarcoma: This is the most common cause of pericardial effusion in dogs, frequently affecting older large-breed dogs (particularly German Shepherd Dogs and Golden Retrievers). It shows a predilection for the right auricle and RA, but may extend along the right AV groove or involve the RV wall (see Figure 6.33a). These masses may also extend into the pericardial space or atrial lumen. Haemangiosarcomas are highly malignant neoplasms of the vascular endothelium and consequently tend to metastasize rapidly. Metastases are frequently present by the time of diagnosis.

Cardiac haemangiosarcomas have been managed with palliative surgery and chemotherapy; however, they are usually associated with systemic spread, particularly splenic and hepatic involvement and pulmonary metastases. The prognosis is poor and pericardiocentesis is often associated with rapid reoccurrence of effusion within days.

Type of effusion	Causes	Features and prognosis
Dogs		
Haemorrhagic (non-clotting, unless acute haemorrhage)	Haemangiosarcoma	Most frequent cause of pericardial effusion affecting the right atrium and right auricle. Older large-breed dogs (German Shepherd Dogs, Golden Retrievers, Labrador Retrievers). Prognosis poor
	Heart base tumour (most commonly chemodectoma)	Most common in brachycephalic breeds. Prognosis fair to good with pericardectomy
	Mesothelioma	Difficult to diagnose even with histology. Prognosis fair with pericardectomy ± chemotherapy
	Idiopathic pericarditis	Medium to large-breed dogs (Golden Retrievers). Prognosis good to excellent with pericardectomy
	Lymphoma	Rare. Effusion can be haemorrhagic–serosanguineous or transudative
	Left atrial rupture	Severe MMVD. Small-breed dogs. Prognosis poor
	Coagulopathy	Rare
	Trauma	
Transudate	Congestive heart failure	Generally small-volume effusion, cardiac tamponade is rare
	Hypoalbuminaemia	
	Toxaemia (e.g. uraemia)	
Exudate	Migrating foreign body	
	Penetrating wounds	
	Leptospirosis, distemper, uraemia	Sterile exudative effusion
Cats		
Pericardial effusions in cats are typically mild and tamponade is rare, so pericardial fluid analysis is generally not pursued. Tamponade is more likely with neoplasia or infectious causes (e.g. feline infectious peritonitis)		
Transudate	Congestive heart failure	Most common cause in cats. Most frequently described in HCM > UCM > RCM. Prognosis guarded to poor
Haemorrhagic	Neoplasia (e.g. lymphoma)	Effusion can be haemorrhagic–serosanguineous or transudative. Most frequent cause after congestive heart failure. Prognosis for lymphoma occasionally reasonable with chemotherapy
Exudate	Feline infectious peritonitis	Sterile exudative effusions. Feline infectious peritonitis is the third most common cause of pericardial effusion in cats
	Toxoplasmosis	
	Systemic infection	

6.36 Potential causes, features and prognosis of pericardial effusions in dogs and cats. HCM = hypertrophic cardiomyopathy; MMVD = myxomatous mitral valve disease; RCM = restrictive cardiomyopathy; UCM = unclassified cardiomyopathy.

Heart base tumours: These are typically chemodectomas and are usually associated with the ascending aorta. Common breeds affected include Boxers, Boston Terriers and English Bulldogs. It has been suggested that these tumours may develop more frequently in brachycephalic breeds due to chronic hypoxia. They may appear as a mass adherent to the aorta or as a large mass arching over the heart base and encompassing the great vessels (see Figure 6.33b). Heart base tumours are usually slow-growing and benign, although some may be more aggressive, such as ectopic thyroid tumours. Surgical debulking has been reported in association with pericardectomy, but pericardectomy alone is associated with a good prognosis. In one retrospective study, median survival in dogs with chemodectoma following pericardectomy was 730 days (Ehrhart *et al*., 2002).

Mesothelioma: This is a diffuse neoplasm of the pericardium and sometimes the pleural surfaces. Mesothelioma may be extremely difficult to diagnose even with histological samples, and it is very difficult to distinguish pericardial effusion secondary to mesothelioma from idiopathic pericardial effusion. Rarely, discrete cardiac masses may be seen. It is possible that chronic inflammatory changes within the pericardium (e.g. due to chronic or recurrent effusion) may predispose to mesothelioma development. Prognosis is fair, with reported survival times of 4–9 months with pericardectomy and 14 months with pericardectomy plus chemotherapy.

Idiopathic pericarditis

Idiopathic pericardial effusion is a diagnosis of exclusion. Many cases are classified as idiopathic because no infectious, immune or neoplastic cause can be identified. Exclusion of alternative causes usually requires comprehensive echocardiography and pericardial fluid assessment, and may also involve exploratory thoracotomy or thoracoscopy and pericardial biopsy. Golden Retrievers and large breeds may be predisposed to the development of idiopathic pericarditis.

Idiopathic effusions may resolve completely following drainage and never recur. However, in a significant number of cases effusion redevelops. If effusion recurs, this should not be immediately attributed to an underlying neoplastic cause, although this is often impossible to exclude. Recurrent idiopathic effusions are best managed with pericardectomy. Prognosis is good to excellent.

There is no difference between neoplastic and non-neoplastic causes in the incidence of bicavitary effusion, ascites or pleural effusion (MacDonald *et al*., 2009). Thus, these signs cannot be used as diagnostic clues or prognostic factors.

Pericardial effusions in cats

CHF is the most common cause of pericardial effusion in cats (see Figure 6.36). CHF-associated pericardial effusion is generally mild and not haemodynamically relevant. Other less frequent causes of pericardial effusion include neoplasia (lymphoma, adenocarcinoma) and feline infectious peritonitis (FIP). Cardiac tamponade is rare in cats, so generally there is no need for pericardiocentesis. Large volumes of pericardial effusion are more likely to be seen with FIP and neoplasia. HCM has been described as the most common cardiomyopathy associated with CHF and pericardial effusion (Hall *et al*., 2007). The prognosis is generally guarded because pericardial effusion is associated with advanced cardiac disease.

Treatment

Haemodynamic support

Pericardial effusion in dogs is rarely secondary to advanced underlying structural heart disease and associated CHF. Thus, diuretics are not indicated. In fact, reduction of circulating blood volume through unnecessary diuresis can exacerbate poor cardiac output by reducing cardiac filling pressures (preload). In an emergency situation, dogs with pericardial effusion and cardiac tamponade may derive short-term benefit from an increase in filling pressures (intravenous fluids as emergency stabilization prior to therapeutic pericardiocentesis). This may seem counterintuitive, as these patients present with clinical signs of right-sided CHF; however, right-sided CHF is a consequence of high intrapericardial pressures with compression of the RA and RV, preventing the venous blood from entering the right heart.

Pericardial drainage

Pericardiocentesis is the treatment of choice whenever there is cardiac tamponade, and this can be both diagnostic and therapeutic. Pericardial drainage may be performed from the right or left side and with the patient in lateral or sternal recumbency (Figures 6.37 and 6.38). The right side is generally recommended because the major coronary arteries are located on the left. A large area is clipped caudal to the elbow, from the 4th to the 8th rib, and a bleb of local anaesthetic (2% lidocaine without adrenaline) is injected slowly whilst the needle is withdrawn from the pleura, through the musculature and subcutis. Ideally, ultrasonography should be used to confirm the diagnosis of pericardial effusion and guide the catheter approach.

Concurrent electrocardiography is useful to help monitor the patient during the procedure and under any sedation. Depending on the underlying pathology, arrhythmias may be common during the procedure. However, during catheter placement, sudden arrhythmias (particularly VPCs) may suggest myocardial irritation by the tip of the catheter, prompting catheter withdrawal and repositioning.

Pericardial effusions can be drained with a large-bore catheter or a specialized pericardial drainage catheter. Safe pericardial catheter insertion requires the patient to be relaxed and still. Thus, there is benefit in providing sedation to minimize stress and discomfort to the patient

- Clippers
- Intravenous catheter for sedatives, emergency general anaesthetics and fluids
- Intravenous fluids
- Butorphanol at 0.2–0.3 mg/kg i.v. alone or in combination with midazolam at 0.2–0.3 mg/kg i.v. for sedation
- 2% lidocaine without adrenaline
- Hibiscrub preparation
- Surgical spirit
- Scalpel blade (No. 11 or 15)
- 14–18 G over-the-needle catheter for dogs (additional side holes can be carefully made with a No. 11 scalpel blade)
- 18–20 G over-the needle catheter or 19 G butterfly needle for cats
- 20 ml (cats) or 50 ml (dogs) syringe
- Three-way stopcock
- Extension tubing
- Kidney dish
- Slides, EDTA tube, plain tube, culture swab
- Ultrasound machine and ECG (ideally)

6.37 Equipment required for pericardiocentesis.

Position

- Left lateral recumbency with right dorsal approach preferred
- Safer – less chance of traumatizing/lacerating coronary artery and lung (approach via the cardiac notch)

Preparation

- Clip a large area of the right thorax caudal to the elbow (from the 4th to the 8th rib and from the sternum to the mid-thorax)
- Identify suitable location for aspiration; use echocardiography to locate a large fluid pocket (typically this will be between the 4th and 6th intercostal space at the level of the costochondral junction)
- Aseptically prepare the site
- Infiltrate lidocaine (inject slowly whilst the needle is withdrawn from the pleura, through the musculature and subcutis)
- Make a very small incision in the skin with the scalpel to prevent burring of the catheter tip as it passes through the skin
- Continuously monitor heart rhythm using an ECG during pericardiocentesis

Pericardiocentesis

1. Insert an over-the-stylet catheter through the skin and muscular layer (in front of the caudal rib of the chosen rib space to avoid the intercostal vessels running caudally to the cranial rib).
2. In patients with pleural effusion, once the catheter enters the thorax, fluid will be seen in the hub (fluid is typically clear). Keep advancing the catheter into the pericardial sac.
3. Pass through the pericardium (can often feel scratching, resistance or a pop). Pericardial fluid will be seen in the hub once the catheter is in the pericardial space, and typically appears bloody. Push the catheter off the stylet and advance into the pericardial sac.
4. Attach a three-way tap with extension tubing for closed collection.
5. Aspirate the pericardial effusion.
6. If the catheter tip touches the epicardium a slight scratch may be felt (ventricular premature contractions may be seen on the ECG). Slightly retract/reposition the catheter.
7. Monitor the ECG throughout the procedure.

Post-pericardiocentesis

- Drain as much fluid as possible, however, remember that:
  - Drainage of even a small amount of fluid is usually beneficial
  - Drainage of pericardial fluid often continues following the procedure via the puncture hole in the pericardium
- Retain fluid samples for cytology ± culture
- Monitor the patient for the following 24 hours using electrocardiography

6.38 Patient positioning and technique for pericardial drainage.

from the procedure (see Figure 6.37). Sedation also reduces the potential for contamination of the pericardial catheter equipment and drainage site.

It has been recommended that correct catheter placement be confirmed by withdrawing fluid into a plain tube and assessing for clotting. Pericardial fluid is typically haemorrhagic but should not clot in a plain tube that is constantly inverted. If the heart has accidentally been punctured, the effusion collected is more likely to clot and significant ventricular arrhythmias are expected. The PCV of pericardial fluid should be less than that of peripheral blood unless an acute pericardial bleed has occurred.

Following pericardial decompression, ascites typically resolves after a couple of days and diuretic therapy is generally unnecessary.

Pericardiocentesis is contraindicated if there is suspected coagulopathy, active pericardial haemorrhage or an atrial tear. Complications of pericardial drainage include arrhythmia, cardiac puncture, coronary artery laceration, pneumothorax, infection and post-procedure discomfort.

Adverse events in the first 48 hours post-pericardiocentesis have been described in 15% of cases, with dysrhythmias being the most common. There was no reported difference in the frequency of adverse events with neoplastic and non-neoplastic causes of effusion, nor with repeated pericardiocentesis, in one study (Humm *et al*., 2009). As arrhythmias were the most frequently reported problem, Humm *et al*. (2009) recommended that, whenever possible, patients be monitored continuously by electrocardiography for at least 24 hours following pericardiocentesis.

Surgery

Surgical management involving exploration and pericardial fenestration or subtotal pericardectomy is indicated in recurrent cases of pericardial effusion, suspected constrictive or infective pericarditis, and suspected heart base tumours or mesothelioma. There is some evidence to suggest improved outcomes in cases managed with thoracotomy (subtotal pericardectomy) and surgical exploration in comparison with minimally invasive thoracoscopic surgery (Case *et al*., 2013). Subtotal pericardectomy via thoracoscopy may yield the same results as thoracotomy, but this needs further investigation.

Cardiac arrhythmias

Bradyarrhythmias

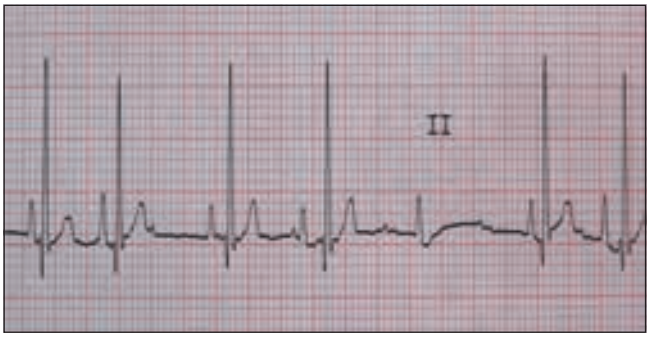
Sinus bradycardia

This is a sinus rhythm that is inappropriately slow for the breed and clinical status of the patient. Generally, sinus bradycardia is not a primary problem but occurs secondary to increased vagal tone due to extra-cardiac disease (e.g. increased intracranial pressure, brachycephalic obstructive airway syndrome, gastrointestinal disease), drugs (e.g. beta-blockers, anaesthetics), hypothermia and electrolyte disturbances (e.g. hyperkalaemia). Clinical signs vary depending on heart rate and range from the absence of signs to weakness and exercise intolerance.

Atropine administration should increase the heart rate if the cause is increased vagal tone, as atropine is a parasympatholytic drug (see below). Treatment is only necessary if the slow heart rate results in low cardiac output and associated clinical signs. If the patient is symptomatic and responsive to atropine, chronic oral anticholinergic (e.g. propantheline bromide) or sympathomimetic (e.g. terbutaline, theophylline) therapy should be provided.

Second-degree atrioventricular block

Second-degree AV block (Figures 6.39 and 6.40) is present when one or more (but not all) atrial impulses fail to conduct to the ventricles due to impaired conduction through the AV node. Second-degree AV block is termed either low-grade or high-grade. High-grade block is



6.39 Lead II ECG recording from a dog with low-grade second-degree atrioventricular block. Note the single blocked P wave. Paper speed 25 mm/s; gain 10 mm/mV.



6.40 Lead I, II and III ECG recording from a dog with high-grade (4:1) second-degree atrioventricular block. Paper speed 50 mm/s; gain 5 mm/mV.

present if the P waves are blocked so frequently at the AV node that two consecutively conducted beats are not evident on the ECG. Second-degree AV block is often described according to the ratio of P waves to QRS complexes (e.g. 3:1 high-grade second-degree AV block means that for every three P waves present, only one conducts through the AV node to generate a QRS complex). Second-degree AV block may also be classified as Mobitz type I (Wenckebach) or type II. In Mobitz type I there is a progressive conduction delay through the AV node before a complete block occurs, which is seen on electrocardiography as a progressive prolongation of the PR interval preceding a blocked P wave. In Mobitz type II the PR interval remains constant and conduction through the AV node is blocked abruptly.

Low-grade second-degree AV block and Mobitz type I block are typically caused by increased vagal tone (secondary to e.g. chronic respiratory disease, neurological disease or gastrointestinal disease). High-grade second-degree AV block and Mobitz type II block are more commonly due to underlying pathology (fibrosis or inflammation) of the cardiac conduction system.

Depending on ventricular rate, there may be no clinical signs or signs of weakness or exercise intolerance. Typically, clinical signs are not present with low-grade second-degree AV block and therefore specific treatment is not necessary. However, the underlying cause of any increased vagal tone should be identified and treated if possible (e.g. chronic respiratory disease or digoxin toxicity).

Clinical signs are more likely with high-grade second-degree AV block. Treatment is warranted if the patient is symptomatic. The response to atropine is usually minimal or absent (see below). Patients with clinical signs (e.g. weakness, syncope) usually have very slow ventricular rates in the presence of high-grade AV block. Treatment should be as for third-degree/complete AV block (see below).

Third-degree or complete atrioventricular block

The sinus node depolarizes the atria but each sinus impulse is blocked at the AV node and cannot reach the ventricles. Maintenance of cardiac output relies solely on slower subsidiary junctional or ventricular pacemaker cells, which depolarize the ventricles to produce 'escape beats' and ventricular contraction (see Figure 6.24).

On the ECG there is no relationship between the P waves and QRS complexes. This is called AV dissociation. Due to this, the PR interval varies and is not consistent. The subsidiary pacemakers in canine AV junctional tissue fire spontaneously at a rate of approximately 40–60 bpm. Those in the ventricular myocardium in dogs typically have a slower escape rate of approximately 20–40 bpm. Cats have higher ventricular escape rates (80–130 bpm). QRS complexes look wide and bizarre. The P waves look normal.

Idiopathic degenerative conduction disease with fibrosis of the AV node is thought to be the mechanism in many cases, since third-degree AV block is mainly seen in older animals. Occasionally, there may be an inflammatory cause (as suggested by spontaneous resolution therapy). This bradyarrhythmia can be associated with hyperthyroidism and cardiomyopathy in cats.

Clinical signs may not be present if the ventricular escape rate remains sufficiently high to maintain adequate cardiac output (50–60 bpm in dogs; 110–130 bpm in cats). However, clinical signs of weakness and syncope may commonly be seen and suggest periods where cardiac output is not adequate. This may occur because the escape rate is low or due to intermittent periods of ventricular asystole – an unstable escape rhythm or paroxysms of ventricular tachycardia, leading to overdrive suppression of the escape rhythm (i.e. after the run of ventricular tachycardia ceases, the ventricular escape rhythm takes a while to start again, during which time there is ventricular asystole).

Clinical signs, if not present at rest, typically occur following mild exertion; it should be remembered that during exercise there is systemic vasodilatation, so in order to maintain systemic blood pressure, ventricular stroke volume and heart rate increase to increase cardiac output. However, if the heart rate is fixed and stroke volume is maximized due to third-degree AV block, exercise will cause a decrease in arterial blood pressure in these patients. If the decrease in blood pressure is severe enough, syncope occurs. Occasionally, patients with third-degree AV block may present with signs of right-sided CHF (especially if the bradycardia has been chronic).

Usually, an atropine response test is negative and medical therapy is typically ineffective at restoring AV nodal conduction, as the problem is not increased vagal tone but rather fibrosis or inflammation. Concurrent inflammatory or infectious diseases should be treated. Permanent pacemaker implantation is the definitive treatment for complete heart block.

Atropine response test

The atropine response test is performed by administering 0.04 mg/kg of atropine subcutaneously and repeating the ECG after 30 minutes. A positive response to atropine is considered to be resolution of the AV block and an increase in the heart rate to >160 bpm

Sick sinus syndrome

Sick sinus syndrome (SSS) (see Figure 6.25) is a conduction system disease involving the sinus node and is thought to be degenerative in nature. Various other regions of the cardiac conduction system can also be diseased (e.g. the AV node and ventricular escape foci).

ECG findings are variable and unpredictable, and can include a combination of some or all of the following:

- Sinus arrest – can often be dramatic with cessation of atrial activity for >8 seconds
- Absence or delay of expected junctional or ventricular escape rhythms
- Supraventricular tachycardia (bradycardia–tachycardia syndrome or tachycardia–bradycardia syndrome)
- Sinus bradycardia.

Dogs with SSS can be asymptomatic or may present with episodic weakness and syncope (the latter is associated with long periods of sinus arrest and asystole). An atropine response test is usually performed to determine whether the bradycardia and sinus arrest are due to elevated vagal tone. Most dogs with SSS have structural conduction disease and typically do not respond appropriately to atropine. However, SSS is highly influenced by autonomic tone; therefore, a partial or even (rarely) full response to atropine in a predisposed breed (West Highland White Terrier, Miniature Schnauzer, Dachshund, Cocker Spaniel) with clinical signs and ECG characteristics suggestive of SSS does not exclude this diagnosis.

If a dog with a partial response does not respond to medical therapy, or if a dog with a negative atropine response test is symptomatic, permanent pacing is the gold standard therapy. Dogs with SSS often do very well with pacing. If a dog has a partial response to atropine (heart rate increases but to <160 bpm), medical therapy can be attempted. This can be in the form of a parasympatholytic drug (e.g. propantheline bromide) or a sympathomimetic drug (e.g. theophylline, terbutaline), or sometimes a combination of the two. Dogs with SSS may experience frequent syncope, which greatly affects the quality of life of these animals and their owners.

Atrial standstill

The diagnosis of atrial standstill (see Figure 6.26) is made when no P waves are evident on any lead of the ECG and the ECG criteria for atrial fibrillation are not met (i.e. slower and more regular rhythm with atrial standstill compared with a faster and more irregular rhythm with atrial fibrillation). P waves are not present on the ECG because the atria cannot be stimulated to be depolarized.

Loss of atrial muscle (atrial myopathy): In this condition the atria, sinus node and internodal tracts are destroyed, presumably by an inflammatory process. The AV junctional tissue takes over the rhythm and the ECG shows a junctional escape rhythm at a rate of about 40–60 bpm. English Springer Spaniels are reportedly predisposed, although this arrhythmia can occur in other breeds as well as occasionally in cats. If atrial standstill is due to loss of atrial muscle, permanent ventricular pacemaker therapy is indicated to control syncope and signs of heart failure. The long-term prognosis has historically been regarded as poor due to the possibility of eventual involvement of the ventricular muscle, but a recent report showed survival times post pacemaker implantation similar to other bradyarrhythmias, suggesting a longer survival than previously speculated (Cervenec *et al*., 2017).

Hyperkalaemia: Atrial myocardium is the tissue most sensitive to hyperkalaemia. Increased extracellular potassium concentration rapidly inhibits the ability of the atrial myocardial tissue to depolarize, before this effect is seen in the rest of the heart. The sinoatrial (SA) node and internodal tracts retain the ability to depolarize until very high potassium levels develop. This results in the SA node still controlling the rhythm, but without atrial depolarization. The resulting rhythm is called a sinoventricular rhythm. If hyperkalaemia is present, this should be urgently addressed (see Chapter 5).

Patients with hyperkalaemia typically have several concomitant abnormalities, such as acid–base imbalances, hypovolaemia and pain, so they are not always bradycardic. Heart rate is not a reliable indirect means of assessing serum potassium levels because a normal or even increased heart rate does not exclude severe hyperkalaemia.

Tachyarrhythmias

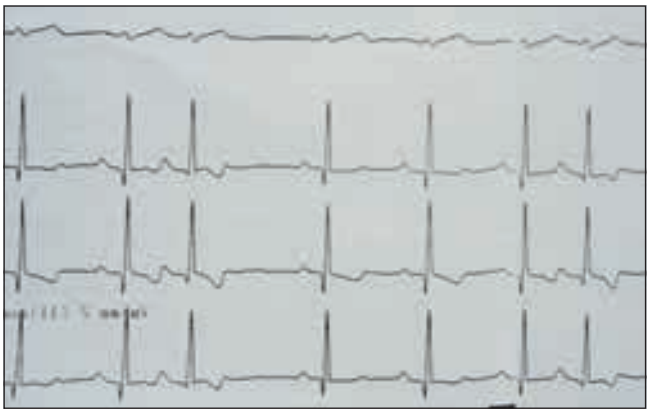
Tachyarrhythmias can be differentiated according to whether the QRS complexes are narrow (i.e. normal width) or wide. Narrow QRS complexes suggest that conduction has occurred via the AV node. Since the location of impulse formation is 'above the ventricle' these rhythms are called supraventricular tachyarrhythmias. Wide QRS complexes generally suggest that the rhythm originated below the AV node and outside of the specialized conduction pathways of the ventricle. Thus, the wave of ventricular depolarization must have travelled from muscle cell to muscle cell, and so resulted in a wide QRS complex. These types of tachyarrhythmias are grouped according to the location of impulse formation as 'ventricular'. It should be borne in mind that supraventricular tachyarrhythmias may occasionally have an aberrant conduction mimicking ventricular tachyarrhythmias.

Sinus tachycardia

Sinus tachycardia is a sinus rhythm at an inappropriately fast rate. This is usually a physiological response to something external and an underlying aetiology can usually be identified. Examples include sympathetic nervous system stimulation (e.g. fear, excitement, pain, fever, hyperthyroidism, hypovolaemia, cardiac tamponade, heart failure, hypoxia, anaemia) and drugs (e.g. catecholamines, atropine, terbutaline, theophylline). Specific treatment is not indicated for sinus tachycardia. If an underlying aetiology is present, this should be addressed.

Supraventricular premature depolarizations

Supraventricular premature depolarizations (Figure 6.41) originate from an abnormal site anywhere above the ventricles. The abnormal site could be in the atrial myocardium or junctional tissue (AV node, bundle of His). Since it may



6.41 Lead I, II and III ECG recording from a dog with two single atrial premature complexes (the 3rd and 7th complexes). Paper speed 50 mm/s; gain 5 mm/mV.

not be possible to distinguish a premature atrial depolarization from a premature junctional depolarization, the term premature supraventricular depolarization is preferred. These single premature depolarizations occur at a faster rate than those from the SA node. Typically, premature depolarizations occur at a rate of >160 bpm.

The premature QRS complex is very similar in appearance to the sinus QRS complex in all ECG leads (because the ventricular depolarization still uses the bundle of His, bundle branches and Purkinje fibres). A P wave may or may not be present and, if present, may or may not be normal in configuration and timing, depending on the site of origin of the supraventricular depolarization.

There are several reasons why a P wave might not be present on the ECG. It may be buried in the previous T wave if the beat is very premature. If the premature depolarization originates in the junctional tissue, retrograde penetration of the atria may or may not occur. If it does occur, it typically happens at the same time as the ventricular depolarization, thus burying the P wave within the QRS complex.

Single premature supraventricular depolarizations do not need to be treated. This arrhythmia is not typically recognized in dogs or cats with a healthy cardiovascular system and therefore its recognition should prompt an investigation into the possibility of cardiac disease. It should also be remembered that non-cardiac diseases, such as electrolyte abnormalities, hypoxia and drug toxicities, can also lead to the development of these arrhythmias.

Supraventricular tachycardia

Supraventricular tachycardia (see Figure 6.21) is usually defined as three or more consecutive premature supraventricular depolarizations in a row. The origin of the supraventricular tachycardia may be atrial or junctional (see above). The QRS complex configuration should be very similar to the normal sinus QRS complex in all ECG leads. The P wave may or may not be present, it may or may not be normal in appearance (positive or negative) and it may occur before, concurrent with or after the QRS complex.

The rate of supraventricular tachycardia in dogs can range from 170 to 350 bpm. Differentiation from sinus tachycardia can be difficult in some cases. Supraventricular tachycardia in dogs is usually associated with underlying cardiac disease and less commonly is due to severe systemic disease. In some rare cases, supraventricular tachycardia may be a primary condition. This type of supraventricular tachycardia is associated with AV conduction over an accessory pathway (re-entrant tachycardia). It is more frequently seen in young animals. These primary arrhythmias may cause secondary myocardial failure if left untreated. The presence of clinical signs depends on the presence of severe underlying myocardial disease and the rate of the supraventricular tachycardia. Supraventricular tachycardia with rates of 250–300 bpm usually causes weakness or collapse, but rarely syncope. Cardiac output is significantly impaired at these high heart rates because diastolic filling time is inadequate. If a dog presents for weakness or collapse secondary to supraventricular tachycardia, this should be addressed as a medical emergency.

Vagal manoeuvres: The vagal tone should be increased to try to slow conduction through the AV node. These manoeuvres can be performed by applying ocular pressure (gently to both eyes) or by carotid sinus massage (gentle massage of the upper neck behind the angle of the jaw) or both.

Precordial thump: This may achieve at least short-term conversion of the supraventricular tachycardia. With the dog in right lateral recumbency, the apex beat is located on the left side of the chest and thumped with the heel of the fist (strength dependent on the size of the patient). This is intended to produce a premature ventricular depolarization that may interrupt the supraventricular tachycardia.

Calcium channel blockers and beta-blockers: Calcium channel blockers (e.g. diltiazem) or beta-blockers (e.g. esmolol) can be administered intravenously. It should be remembered that moderate to severe myocardial failure is a relative contraindication to the administration of beta-blockers due to their negative inotropic effects (i.e. they decrease myocardial contractility).

Atrial fibrillation

Atrial fibrillation (see Figure 6.22) is typically associated with a rapid heart rate (usually >200 bpm) and supraventricular morphology of the QRS complexes (narrow and upright complexes in lead II of the ECG). The rhythm is irregularly irregular and there is no identifiable pattern. P waves cannot be identified. The baseline may have irregular undulations (fibrillation waves). There may be variation in the height of the QRS complexes.

It should be noted that when atrial fibrillation is very rapid (>250 bpm) it may be difficult to identify that the rhythm is irregular. In this situation, identification is aided if a long ECG strip is printed at 50 mm/s so that the R–R irregularities are easier to detect. As a clinical tip, if a rapid irregular supraventricular tachycardia without identifiable P waves is seen, this should be assumed to be atrial fibrillation until proven otherwise.

Atrial contraction contributes about 20–25% to the cardiac output. The loss of atrial contraction due to the development of atrial fibrillation in dogs with serious heart disease can be very detrimental to cardiac output. Stroke volume and cardiac output decline and end-diastolic pressure increases. Clinical deterioration occurs, possibly with the development of CHF. The sustained increase in heart rate can induce further myocardial systolic dysfunction over several weeks (tachycardiomyopathy).

On physical examination, the erratic cardiac rhythm and varying intensity of the heart sounds mean that these patients have distinct auscultation findings (sometimes described as sounding like 'tennis shoes in a tumble dryer'). Patients will also have pulse deficits and variations in pulse quality, as the strength of the pulse depends on the preceding diastolic interval, which varies due to the irregular heart rate. As pulse deficits are common, a heart rate that is derived from the pulse rate is inaccurate. It is also difficult to determine the heart rate via auscultation due to the rapid and irregular nature of the arrhythmia. Thus, it is always best to determine the heart rate from an ECG.

Conversion to sinus rhythm is often not a realistic goal as the presence of severe underlying heart disease usually makes these dogs refractory to successful conversion. Control of the heart rate with medical therapy is usually the treatment of choice in dogs and cats. Drugs that slow AV node conduction are used to slow the ventricular response rate.

Digoxin: This drug is usually the first-line treatment for chronic management in dogs because it is a weak positive inotrope and does not depress contractility. It usually has a mild effect on heart rate and therefore is often not sufficiently effective as a sole antiarrhythmic. Thus, it is often

combined with a second antiarrhythmic drug (e.g. diltiazem) to slow the heart rate further. Digoxin is given orally, as the intravenous route can be associated with unacceptable toxicity. Poor renal perfusion, renal insufficiency and hypokalaemia may predispose to digoxin toxicity. In these cases digoxin should be administrated carefully and serum levels closely monitored. This drug is rarely used in cats, as they are more sensitive to the toxic effects than dogs.

Calcium channel blockers: These drugs slow conduction through the AV node. This drug is usually given either alone or combined with digoxin as first line treatment for atrial fibrillation.

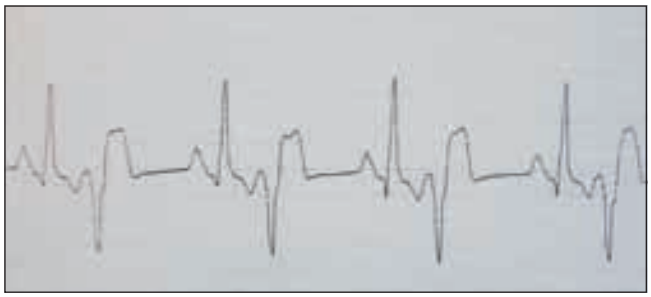
Beta-blockers: These drugs slow conduction through the AV node. Oral therapy is generally used for atrial fibrillation. These drugs can be used either alone or combined with digoxin as an alternative for a digoxin-diltiazem combination. Caution is recommended with the use of beta-blockers when myocardial failure is present. These drugs must be started at a low dose and tapered to a dose that can be tolerated by the patient.

Ventricular premature contractions

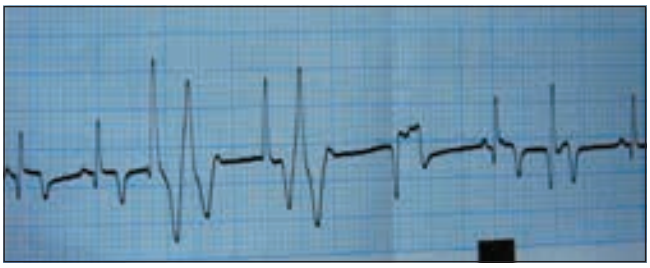
Ventricular premature contractions (VPCs) have wide and bizarre QRS complexes because they originate below the bundle of His (within the ventricle) and therefore the wave of depolarization does not travel through the specialized ventricular conduction system. Instead, it depolarizes the ventricles more slowly, from cell to cell within the ventricular myocardium. The QRS complexes can be positive or negative in lead II of the ECG, depending on the site of origin (right or left ventricle, respectively). There is no P wave associated with the QRS complex of a VPC. The T wave is often large, discordant (i.e. opposite polarity to the QRS complex) and bizarre, reflecting the abnormal repolarization. As the name suggests, the timing of the VPC is premature relative to the underlying sinus rhythm.

VPCs can occur in patterns such as ventricular bigeminy, where every second beat is a VPC (Figure 6.42), or ventricular trigeminy, where every third beat is a VPC. If the VPC occurs on the downslope of the T wave of the preceding beat, it is referred to as R-on-T phenomenon (Figure 6.43). The downslope of the T wave is a vulnerable period, and depolarization during this time may predispose to ventricular fibrillation. This is an important ECG feature to recognize, as R-on-T phenomenon requires prompt, aggressive antiarrhythmic therapy.

VPCs can occur in normal animals in low numbers. VPCs also occur commonly in association with non-cardiac diseases (e.g. gastric dilatation–volvulus, splenic disease and following surgery). VPCs secondary to systemic disease often tend to be self-limiting if the underlying disease is addressed. It appears that in dogs with VPCs and no underlying heart disease, the number of VPCs is not predictive of the risk of sudden death (and the actual risk appears to be low).



6.42 Lead II ECG recording from a dog. Every sinus complex is followed by a ventricular premature complex in a repeating pattern. This is called ventricular bigeminy. Paper speed 50 mm/s; gain 10 mm/mV.



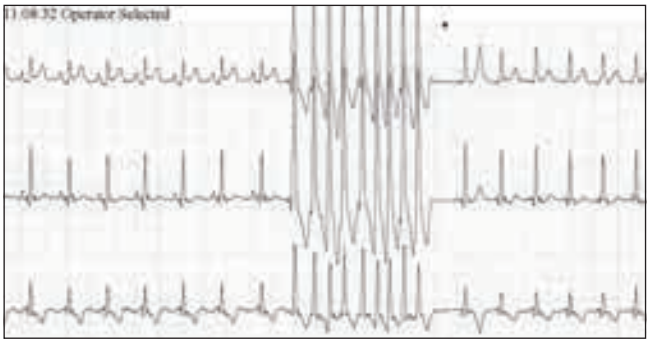
6.43 Lead II ECG recording from a dog. These close-coupled ventricular premature contractions show R-on-T phenomenon. Paper speed 25 mm/s; gain 10 mm/mV.

VPCs can also be associated with primary myocardial diseases (particularly DCM in Dobermanns and ARVC in Boxers). Dogs with single VPCs on the ECG and suspicion or evidence of underlying myocardial disease warrant further monitoring (e.g. Holter monitoring or telemetry) to determine whether more serious arrhythmias are occurring at other times. Clinical signs do not occur with single VPCs. Thus, in a patient without clinical signs, the rationale behind treatment is to attempt to prevent sudden death. However, the ability to predict the likelihood of sudden death associated with VPCs in an individual patient is poor.

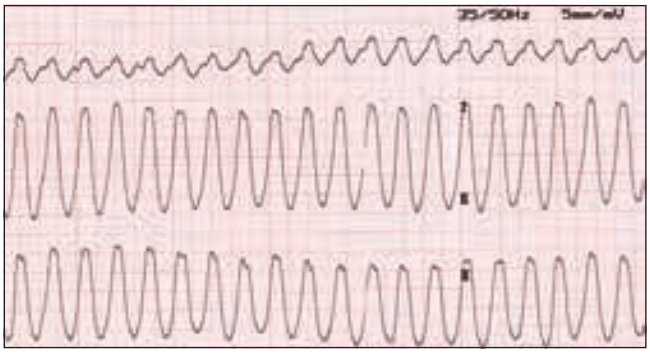
If deemed necessary, the antiarrhythmic treatment for frequent VPCs is the same as for ventricular tachycardias.

Ventricular tachycardia

In ventricular tachycardia (Figures 6.44 and 6.45) the morphology of the QRS complexes is wide and bizarre. The shape and polarity of the QRS complex depends on the origin of the ectopic ventricular depolarization (i.e. right or left ventricle) and the intraventricular conduction pathway. Ventricular tachycardia can be monomorphic (all QRS complexes have the same appearance/morphology) or polymorphic (several different QRS complex morphologies). The latter might imply multifocal ventricular origins for the arrhythmia. Most ventricular tachycardias are regular. When describing the frequency of VPCs, a ventricular couplet is two consecutive VPCs, a ventricular triplet is three consecutive VPCs and ventricular tachycardia is more than three consecutive VPCs. Ventricular tachycardia is sustained if it lasts >30 seconds and non-sustained if it lasts <30 seconds.



6.44 Lead I, II and III ECG recording from a cat. There is a short paroxysm of ventricular tachycardia lasting for nine beats. Paper speed 25 mm/s; gain 20 mm/mV.



6.45 Lead I, II and III ECG recording from a dog with a fast, regular, wide QRS complex tachycardia (QRS width >70 ms). The dog was in sustained ventricular tachycardia at a rate of 370 bpm. Paper speed 50 mm/s; gain 5 mm/mV.

Ventricular tachycardia* versus *accelerated idioventricular rhythm: A ventricular rhythm with a rate <140–170 bpm (approximately) is termed an accelerated idioventricular rhythm (AIVR) (Figure 6.46), as it is not fast enough to be a true ventricular tachycardia. A true ventricular tachycardia is a ventricular rhythm at a rate >170 bpm.

AIVRs are encountered commonly in hospitalized patients with non-cardiac diseases (gastric dilatation–volvulus surgery, splenic disease, pancreatitis, prostatitis, post-trauma and neurological diseases). These rhythms are often benign and the rate is slow enough not to compromise cardiac output. They typically do not require antiarrhythmic therapy, as they tend to be self-limiting when the underlying systemic disease is addressed.

If the rate of the ventricular tachycardia is rapid (e.g. >250–300 bpm), signs of poor cardiac output may be present or syncope may occur. If the rate of the ventricular tachycardia is <200 bpm, clinical signs may not be present, although, ultimately, the presence of clinical signs is also influenced by the degree of underlying structural heart disease.

The goals of treatment are to improve haemodynamics and to minimize the risk of sudden death. As all antiarrhythmic treatment carries risks of side effects, the decision to instigate therapy must be made carefully. The following considerations should be kept in mind:

- Is the arrhythmia causing haemodynamic compromise? If it is not, then even if the ECG looks abnormal, treatment may not be necessary and close monitoring of the arrhythmia may be the best option. The presence or absence of underlying cardiac disease is an important factor in determining whether an arrhythmia is causing significant compromise.



6.46 Lead I, II and III ECG recording from a dog with an accelerated idioventricular rhythm (AIVR). The AIVR competes with the underlying sinus rhythm as the rate of each rhythm is similar. Paper speed 50 mm/s; gain 5 mm/mV.

  A structurally normal, healthy heart can tolerate arrhythmias for some time, whereas a diseased heart cannot. Peripheral pulse quality, mucous membrane colour, attitude of the patient and arterial blood pressure should be evaluated. Sustained ventricular tachycardia at a high rate is more likely to cause haemodynamic compromise than ventricular tachycardia at slower rates
- Is the arrhythmia likely to degenerate into ventricular fibrillation, which will cause sudden death? The presence or absence of underlying cardiac disease is important, since a healthy heart can tolerate more than a diseased heart. The faster the ventricular tachycardia, the more likely that a premature depolarization will fall within the vulnerable period of the T wave and induce ventricular fibrillation (R-on-T phenomenon). Polymorphic ventricular tachycardia is thought to be more dangerous than monomorphic ventricular tachycardia.

Certain patient groups appear to have an increased risk of sudden death associated with ventricular tachycardia, including:

- Dobermanns with DCM
- Boxers with ARVC (formerly known as Boxer cardiomyopathy)
- Dogs with severe subaortic stenosis and associated LV myocardial hypertrophy, ischaemia and fibrosis
- Cats with HCM.

The first priority for treatment is to ensure that the patient is hydrated and that oxygenation, acid–base status, haematocrit and electrolyte concentrations are normal. Once the decision has been made to instigate drug therapy, there are a number of options available.

Lidocaine: This is the initial drug of choice. Lidocaine is a class IB antiarrhythmic drug (blocks fast sodium channels) and is only available for intravenous use. It is given as a bolus or as a CRI (see Figure 6.32). It may be less effective in the presence of hypokalaemia, when an incorrect diagnosis has been made (lidocaine is generally ineffective for the treatment of supraventricular arrhythmias) or if an inappropriately low dose is used.

It is rare for ventricular tachycardia to show no response to lidocaine, but AIVRs may not respond well to lidocaine administration. The slower the ventricular tachycardia, the less likely it is to respond. It should be noted that a 'response' may simply be a slowing of the ventricular tachycardia and not an actual cessation. Toxicity to lidocaine at high doses manifests as neurological signs (e.g. seizures), hypotension and gastrointestinal signs (e.g. vomiting); cats are more sensitive to lidocaine toxicity.

If there is no response to the first lidocaine bolus of 2 mg/kg, the administration should be repeated 2–3 times, to a maximum of 8 mg/kg within 10 minutes. Once a response is seen, a CRI of lidocaine can be started (see Figure 6.32). If after the administration of 8 mg/kg of lidocaine there has been no conversion to sinus rhythm or decrease in the rate of the ventricular tachycardia, the clinician should look for electrolyte imbalances, reassess the ECG to confirm the diagnosis (i.e. is this supraventricular tachycardia with aberrant ventricular conduction mimicking a ventricular tachycardia?) and check whether the intravenous catheter is still in place. If lidocaine fails to convert the ventricular tachycardia, second-line drug choices can be considered. There is no general consensus

of which drug is the best choice after lidocaine. Sotalol or amiodarone ± magnesium sulphate would be the typical choices if there is a failure of ventricular tachycardia to respond to lidocaine.

Procainamide: This drug can be tried (intravenously) if lidocaine is ineffective (see Figure 6.32).

Beta-blockers: These drugs can be tried (intravenously), but they should be avoided or used very cautiously in cases of systolic dysfunction. They should not be used in cases of advanced MMVD or DCM, as these patients are highly dependent on adrenergic tone to maintain cardiac output and may become severely hypotensive.

Magnesium: This may be effective in some cases and is worth using in cases of refractory ventricular tachycardia. Magnesium should be administered slowly intravenously (see Figure 6.32). Adverse effects such as vomiting and salivation may be observed if given too rapidly.

Sotalol: This drug has been shown to be effective for the reduction of ventricular tachycardia in Boxers with ARVC. It can be administered orally or intravenously. Since sotalol also has some beta-blocking properties it must be used with caution in dogs with myocardial failure (see Figure 6.32).

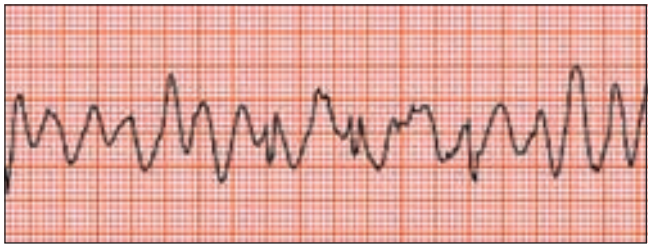
Amiodarone: The use of amiodarone has been reported. When given intravenously, it may cause hypotension and anaphylactic-like reactions due to the solvent used in most preparations (polysorbate 80). These preparations should be avoided. A new preparation of amiodarone that does not contain polysorbate 80 (Nexterone) has recently become available and has been shown to be safe (Levy *et al*., 2016).

Chronic therapy: The agent of choice for chronic oral drug therapy, after the patient has been stabilized, should ideally be the one that converted the ventricular tachycardia. Mexiletine is an oral class IB drug (similar to lidocaine) and can be used as monotherapy or in combination with atenolol or sotalol with generally very good results.

Other options: Direct current cardioversion may be tried as a last resort in cases of drug-resistant ventricular tachycardia.

Ventricular fibrillation

Ventricular fibrillation (Figure 6.47) occurs as a pre-terminal event (cardiac arrest) where ventricular electrical activity is chaotic and no organized ventricular contractions occur.



6.47 Lead II ECG recording from a dog that had a cardiac arrest during anaesthesia. There are irregular baseline undulations with no discernible P, QRS or T waves. The dog was in ventricular fibrillation. Paper speed 25 mm/s, 10 mm/mV.

If not treated, ventricular fibrillation will result in death. The ECG comprises irregular baseline undulations with no discernible P, QRS or T waves. It is important to ensure that this is not an artefact: the ECG leads should be checked to ensure that they are properly attached, as lack of electrode contact of the skin can mimic ventricular fibrillation. The only effective method of treatment for ventricular fibrillation is electrical defibrillation. The chance of conversion to sinus rhythm depends on the clinical situation. A healthy dog with anaesthetic complications causing the ventricular fibrillation stands a good chance of successful defibrillation. A dog with severe systemic or cardiac disease has a very poor chance of conversion.

Summary of therapeutic considerations for tachyarrhythmias

The need for antiarrhythmic treatment should first be determined based on the presence of clinical signs. Electrolyte, acid–base, oxygenation, hydration and haematocrit abnormalities should be corrected. Consideration should be given as to whether myocardial function is normal or abnormal, as a structurally normal heart can tolerate arrhythmias better than a diseased heart. It should be borne in mind that most antiarrhythmic drugs have negative inotropic actions, which may cause decompensation in a patient with severe myocardial failure.

The likelihood that an arrhythmia could degenerate into a fatal arrhythmia is often difficult to predict. Typically, the faster the arrhythmia, the more dangerous it is. Polymorphism is thought to be more malignant that monomorphism. Paroxysms and/or runs of ventricular tachycardia are much more dangerous than single abnormal beats. Ventricular arrhythmias are more likely to cause a fatal arrhythmia than supraventricular arrhythmias. In breeds with certain diseases (e.g. ARVC in Boxers, DCM in Dobermanns, severe subaortic stenosis in dogs and HCM in cats), ventricular arrhythmias are thought to carry a particularly high risk.

Arrhythmias that are of minimal concern and usually do not require antiarrhythmic therapy include single supraventricular complexes and single ventricular complexes. Arrhythmias that are probably not dangerous and usually do not require antiarrhythmic therapy include AIVRs. Arrhythmias that are the most cause for concern and require antiarrhythmic therapy include rapid, non-sustained or sustained ventricular tachycardias and supraventricular tachycardias.

Regular monitoring is needed with all antiarrhythmic therapy to ensure efficacy and that the arrhythmia has not been exacerbated by the treatment. It is important to remember that any antiarrhythmic agent can also be proarrhythmic. Antiarrhythmic medication can be expensive and regular follow-up evaluations with electrocardiography and Holter monitoring are typically necessary. The owner must be able to administer the oral medication at the required dosing interval, potentially on a long-term basis (depending on the underlying cause of the arrhythmia).

Arterial thromboembolism

Key points

- Typical clinical signs: acute onset, often no previous history of a cardiac disease, hindlimbs more frequently affected than forelimbs, five 'Ps' – paralysis/paresis, pain, pulselessness, pallor (or cyanotic nail beds and footpads), polar (cold distal limbs and footpads). Cats are frequently tachypnoeic or may even show open-mouth breathing. In dogs, arterial thrombosis has generally a more chronic progression and is not associated with cardiac disease.
- Diagnosis: physical examination findings are highly suggestive of arterial thromboembolism (ATE). On U-SEE examination, a RPLA or RPSA typically reveals an enlarged LA in cats and 'smoke' or a thrombus may additionally be present. Such findings are consistent with cardiogenic ATE. Tachypnoea/dyspnoea is frequently caused by stress and pain, and not necessarily pulmonary oedema. Thoracic radiographs should be obtained to confirm the presence of pulmonary oedema.
- Differential diagnoses: trauma, neurological diseases (e.g. brachial plexus avulsion, intervertebral disc extrusion).
- Treatment: opioid analgesia is the first priority, followed by anticoagulation therapy and CHF therapy (if pulmonary oedema is present).
- Prognosis: factors associated with a poor prognosis include bilateral rear limb involvement, no motor activity and hypothermia (<37.2°C).

ATE is most frequently seen in cats and is one of the most serious complications associated with feline cardiomyopathies. In dogs, ATE is rare and not usually associated with cardiac disease. Thrombosis represents clot formation within a cardiac chamber or vascular lumen and thromboembolization occurs when a clot or part of it embolizes from the site where it was formed and lodges within a vessel. In cats, thrombi are most frequently located in the LA and left auricle. Right-sided cardiac and deep vein thromboses are rare in dogs and cats compared with humans. Most frequently, emboli form in the left side of the heart and lodge in the distal aorta (termed 'saddle thrombi') but can also occlude the brachial, renal, coronary, cerebral and mesenteric arteries.

ATE can occur in cats with any type of cardiomyopathy, but is most commonly seen with HCM. The large majority of cats with ATE also have advanced heart disease, although in some cases no underlying heart disease is present. In these patients, the most frequent cause of ATE is neoplasia (particularly pulmonary carcinoma). Other differential diagnoses include protein-losing enteropathy/nephropathy, recent administration of corticosteroids and endocarditis. Occasionally, no cause for ATE is found. Hyperthyroidism has been diagnosed in some cats with ATE and, in general, these cats have thyroid-induced cardiac changes that are likely to be responsible for the cardiogenic thromboembolism. However, in a small percentage of hyperthyroid cats with ATE, no structural heart disease is identified, so it is unclear whether hyperthyroidism *per se* is a risk factor for ATE.

In dogs, ATE has been described in association with neoplasia, protein-losing enteropathy/nephropathy, recent administration of corticosteroids, hyperadrenocorticism, immune-mediated haemolytic anaemia and endocarditis. Occasionally, no underlying cause can be found, which may suggest thrombus formation *in situ* rather than a thromboembolic event.

Thrombosis occurs whenever one or more of three essential conditions (Virchow's triad) are present. These are:

- Local vessel or tissue injury
- Circulatory stasis
- Altered blood coagulability (hypercoagulable state).

In the first instance, a damaged endothelial wall induces platelet adhesion and aggregation, activating the clotting cascade (see Chapter 13). Circulatory stasis occurs typically in the face of an enlarged LA and/or left auricle due to diastolic/systolic impairment and poor atrial emptying (seen as 'smoke' on echocardiography). It has been suggested that cats with cardiomyopathy may be hypercoagulable (Bedard *et al*., 2007; Stokol *et al*., 2008); in part this may be because feline platelets are very reactive and platelet reactivity may be exacerbated in cardiomyopathic patients (Helenski and Ross, 1987; Welles *et al*., 1994). However, not all cats with ATE are hypercoagulable (Stokol *et al*., 2008), so this is not the primary factor predisposing cats to thrombosis. The main thrombogenic factor in feline cardiomyopathy is likely to be the presence of circulatory stasis as a result of a significantly dilated LA with decreased systolic function. This is why a dilated LA is an indication for starting prophylactic anticoagulation therapy in cats.

The primary pathophysiological mechanism in ATE is arterial obstruction caused by the thrombus. In addition to the physical obstruction, the clot releases several vasoactive substances (serotonin, prostaglandins, thromboxane A2) that cause vasoconstriction of the collateral circulation. These vasoactive substances play a critical role in the progression and resolution of clinical thromboembolic disease. Sudden complete arterial occlusion, coupled with decreased collateral circulation, causes substantial ischaemic tissue and nerve injury.

Clinical consequences of ATE are dependent on several factors: the site of the arterial obstruction (distal aorta, brachial artery or other sites such as the cerebral, renal and mesenteric arteries); functional patency of the collateral circulation; the duration and completeness of obstruction; and development of serious complications (e.g. self-mutilation, limb necrosis, hyperkalaemia).

Diagnosis

History

The history often includes peracute onset of clinical signs that can be mistaken for trauma or neurological disease. There is often no previous history of heart disease; ATE may be the first clinical sign of an underlying cardiac condition. Sudden death is also a possible initial clinical finding.

Clinical signs and physical examination

The clinical signs and physical examination findings depend on the specific tissues and/or organs that are embolized. Hindlimb paresis/paralysis (unilateral or bilateral) from distal ATE ('saddle thrombus') is the most common presentation; in cats, both hindlimbs are affected in

the majority of cases (Smith *et al*., 2003). Forelimb paresis/paralysis can occur due to brachial artery thromboembolism. Some studies have suggested that the right forelimb is more frequently affected than the left forelimb, although a large retrospective study showed a similar frequency of ATE in both forelimbs (Smith *et al*., 2003). In rare cases where mesenteric, renal or cerebral arteries are embolized, bloody diarrhoea, acute renal failure or seizures may be observed respectively.

Thromboemboli affecting the extremities result in clinical signs that relate to the five 'Ps':

- Paralysis/paresis (Figure 6.48a)
- Pain
- 'Pulselessness'
- Pallor (nail beds and footpads may be pale or cyanotic) (Figure 6.48b)
- Polar (cold distal limbs and footpads).

With 'saddle' thrombus, the cranial tibial and gastrocnemius muscles become firm from ischaemic myopathy by 10–12 hours post-embolization, becoming softer 24–72 hours later. Most cats show severe pain if the limbs are manipulated. Occasionally, cats may appear to be pain-free; this can be due to long-standing ischaemia with subsequent neuropathy and loss of pain sensation. Vocalization is common due to pain and distress. Hypothermia may occur and is a poor prognostic indicator in both forelimb and hindlimb ATE.

Dyspnoea, tachypnoea and syncope may also be present due to CHF. However, tachypnoea, open-mouth breathing and abnormal respiration patterns are present in the large majority of cases and do not necessarily reflect CHF. In a large retrospective study of ATE, 90% of cats were tachypnoeic but only 44% had radiographic evidence of CHF (Smith *et al*., 2003). Thus, in ATE, respiratory rate does not discriminate between cats with and without CHF. Increased respiratory rate in ATE is often caused by pain and/or acid–base imbalances.



6.48 (a) Cat with left forelimb monoplegia due to arterial thromboembolism. (b) There is marked cyanosis of the footpads of the affected limb.
(Courtesy of Dr T Glaus)

Thoracic auscultation

Thoracic auscultation often reveals tachycardia, which can be due to pain, stress, acid–base imbalances or CHF (it should be remembered that an increased heart rate is not always seen in cats with CHF). A gallop sound or arrhythmia suggests the presence of cardiac disease and supports a suspicion of cardiogenic ATE. A cardiac murmur may be suggestive of underlying cardiac disease in cats with ATE (but it should be borne in mind that normal cats may have heart murmurs, which makes this finding less specific). Normal cardiac auscultation does not rule out ATE and can be present in up to 40% of affected cats (Smith *et al*., 2003). Pulmonary crackles may be detected in some cats with severe pulmonary oedema; however, they are often not audible even in patients with radiographic evidence of significant pulmonary oedema. Muffled heart and lung sounds may be caused by pleural effusion in cases of CHF.

U-SEE examination

Echocardiography: This should be performed to assess LA size and to determine whether 'smoke' or a thrombus is present. Any of these findings is strongly suggestive of ATE in the face of typical clinical signs. The LA is usually markedly enlarged in cases of ATE in cats. If the size of the LA is normal (<16 mm on a RPLA view or LA/Ao <1.6 on a RPSA view), cardiogenic ATE is unlikely. However, if the suspicion for ATE is still high, further diagnostics are required to rule out other non-cardiac causes of thromboembolism (e.g. thoracic radiographs to assess for pulmonary neoplasia).

PRACTICAL TIPS

- A RPSA view should be used to carefully examine the left auricle for the presence of 'smoke' and/or a thrombus
- Slightly increasing the gain setting on the echocardiographic machine may help identify 'smoke' (see Figure 6.14)

The presence of 'smoke' is associated with blood stasis and considered to be a marker for increased thromboembolic risk. A thrombus may be visible as a hyperechogenic structure floating freely within the LA, or it may be attached, typically to the wall of the left auricle (see Figure 6.14). The low blood flow velocity in a dilated and hypokinetic left auricle makes it the ideal location for thrombus formation.

The thorax should be examined for pleural effusion, which may be present in cases of ATE and concurrent CHF. The abdominal aorta may be evaluated for the presence of a thrombus if the diagnosis is unclear or to confirm distal aortic thromboembolism (see Figure 6.20).

Electrocardiography: This can be used to identify abnormalities in ATE cases; some abnormalities are benign but others are highly malignant and require intervention. Prompt recognition of these ECG abnormalities is mandatory.

- Malignant ECG findings: ventricular tachycardia, sustained supraventricular tachycardia or atrial standstill (secondary to hyperkalaemia as a result of reperfusion injury or acute renal failure secondary to renal thromboembolism) (see Figure 6.26). Emergency treatment is necessary. It should be remembered that a patient with severe hyperkalaemia is not always bradycardic. Heart rate is not a reliable indicator of hyperkalaemia.

Thoracic radiography

Thoracic radiography usually reveals cardiomegaly. The diagnosis of CHF (particularly the presence of pulmonary oedema) in ATE cases should not be purely based on respiration rate and/or effort. Thoracic radiography is necessary to confirm the presence of lung oedema.

Clinical pathology

Abnormalities in most cases include hyperglycaemia, azotaemia and increased creatine kinase (CK) and aspartate aminotransferase (AST) consistent with widespread muscle cell injury. Azotaemia is generally pre-renal due to dehydration and/or hypotension. Renal azotaemia may occur in cases of renal thromboembolism, although this tends to be more severe and progressive. CK is typically significantly elevated in all cases of ATE and is highly sensitive (although not 100% specific because trauma and muscular disease can also cause elevations in CK). Other biochemistry abnormalities that may be observed include hyperkalaemia, increased alanine aminotransferase (ALT), hyperphosphataemia and hypocalcaemia. Analysis of acid–base balance usually reveals metabolic acidosis associated with reperfusion injury.

Peripheral venous glucose and lactate concentrations may be measured in the affected limbs to help in the diagnosis of ATE. This may be useful in cases where the physical examination findings are not completely typical for ATE (e.g. in cases with thromboembolism and partial arterial occlusion). Local glucose and lactate levels are expected to be lower and higher, respectively, in comparison with central venous levels. The difference between the central and peripheral (affected limb) blood glucose concentration (ΔGlu) has been suggested to predict ATE with a high sensitivity and specificity using the proposed cut-off values of ΔGlu ≥2–5 g/l in cats and ΔGlu ≥1.6 mmol in dogs (Klainbart *et al*., 2014).

Blood flow assessment

Blood flow in the affected limb can be assessed by cutting the nail to the quick to check for bleeding, or by using Doppler ultrasonography to detect blood flow in the artery. Measuring venous blood glucose and lactate concentrations in the affected limb(s) may also be useful for assessing flow.

Differential diagnoses

The differential diagnoses for acute posterior paresis include trauma, intervertebral disc extrusion, spinal lymphoma or other neoplasms, and fibrocartilaginous embolism. Differential diagnoses for acute forelimb monoparesis include trauma and brachial plexus avulsion.

Treatment for acute episodes

In addition to the treatment for acute episodes of ATE (described below), CHF and serious cardiac arrhythmias must be managed when present. However, before initiating emergency CHF therapy, it is important to confirm that the patient is actually in CHF. Thoracic radiographs should be obtained if the patient is stable. Diuretics and/or vasodilators should only be administered once the presence of CHF has been confirmed because these drugs may cause hypotension and hypovolaemia, which can further compromise the peripheral circulation in patients with ATE.

Analgesia

Pain control is one of the first therapeutic goals in the management of acute ATE in cats and is mandatory for at least the first 24–48 hours. Later in the course of ATE, ischaemic neuropathy may develop causing pain sensation to be reduced. It should be remembered that pain may be very difficult to assess in this situation and that cats in severe pain may just appear lethargic. In all cases of ATE, pain should be assumed to be present and analgesia provided.

Opioids are the best choice in this situation. Butorphanol is too weak as an analgesic and should not be used. Fentanyl (2–5 μg/kg slow i.v. followed by a CRI of 2–5 μg/kg/h (micrograms/kg/hr)) or methadone (0.2–0.4 mg/kg slow i.v., i.m. q4–6h) are the best choices. Buprenorphine (0.02–0.03 mg/kg i.v., i.m. q6h) can be considered, but in cases of severe pain the analgesic effect of buprenorphine may not be sufficient. Intramuscular injections should not be given in the affected, unperfused limbs. Non-steroidal anti-inflammatory drugs (NSAIDs) should be avoided, as these patients are typically dehydrated and may be hypotensive, which can compromise renal perfusion and function.

Anticoagulation therapy

Anticoagulant drugs have no effect on established thrombi, but can help to prevent further thrombus formation from the activated blood clotting pathways. There are little published data on the efficacy of anticoagulant therapy in cats. An increased risk of bleeding is a potential major complication, although the risk appears to be small. However, clotting profiles should be monitored wherever possible.

Unfractionated heparin may be used. It binds to plasma antithrombin to neutralize thrombin and activated Factors XII, XI, X and IX, preventing activation of the clotting cascade. Published doses vary widely: an initial dose of 200–300 IU/kg i.v. followed by 250–300 IU/kg s.c. q8h has been suggested (Greene and Meriwether, 1982). Adjustment of this dose should then be performed with the proposed goal of prolonging the activated partial thromboplastin time (aPTT) to 1.5–2.0 times pre-treatment values. Unfractionated heparin should not be administered intramuscularly due to the risk of local haemorrhage.

More recently, the use of low molecular weight heparin (LMWH) has been suggested as an alternative to unfractionated heparin. LMWH is derived from de-polymerization of unfractionated heparin. LMWH maintains the ability to inhibit activation of Factor X, but affects thrombin minimally. Cats appear to have rapid absorption and elimination kinetics for LMWH and require more frequent dosing compared with humans. Thus, the current recommendations for enoxaparin (1–2 mg/kg s.c. q12–24h) and dalteparin (100–200 IU/kg s.c. q12–24h) may not be adequate for all cats. Many cats seem to require at least q8h treatment, and recent studies in normal cats suggest q6h protocols (Mischke *et al*., 2014; Schönig and Mischke, 2016). Furthermore, as thrombin is not affected by LMWH, measurement of aPTT is no longer useful for monitoring

efficacy of treatment; monitoring of anti-FXa levels is recommended when initiating therapy. The 'target' anti-FXa level in healthy cats and cats prone to ATE is unknown. Further research is required in this area.

Anti-platelet therapy

Anti-platelet therapy may be provided concurrently with anticoagulation treatment once the patient is eating, or may be used as the sole anticoagulation therapy. Aspirin is a cyclooxygenase (COX)-1 inhibitor, which causes thromboxane A2 inhibition. Thromboxane A2 is needed for platelet recruitment and activation and is a potent vasoconstrictor. Reduction of thromboxane A2 may help improve the collateral circulation and, by modifying platelet aggregation, may prevent further thrombus formation. There is no difference in the survival or recurrence rate in cats receiving a high dose (>40 mg/cat) or a low dose (5 mg/cat) of aspirin (Smith *et al*., 2003). The high dose of aspirin is associated with more frequent gastrointestinal adverse effects. The recommended dose for cats (taking into consideration the preparations of aspirin available in the UK) is 18.75 mg/cat (¼ of a 75 mg tablet) orally q72h.

Clopidogrel is an adenosine diphosphate (ADP) receptor antagonist that prevents primary and secondary platelet aggregation. It also reduces the release of serotonin and thus is potentially helpful in promoting collateral circulation. The recommended dose for cats is 18.75 mg/cat orally q24h (¼ of a 75 mg tablet). A recent trial comparing the efficacy of clopidogrel and aspirin in reducing ATE recurrence showed a significant decrease in recurrence rate and longer time to recurrence in the group of cats receiving clopidogrel (Hogan *et al*., 2015). Based on these data, it appears that clopidogrel is more efficacious than aspirin and should be the first choice for thromboprophylaxis. Aspirin and clopidogrel have an additive effect in humans, preventing platelet aggregation through two separate pathways. No studies in veterinary medicine have evaluated the efficacy of this combination in cats, although the benefit seems likely and the risk of haemorrhage is low.

Thrombolytic therapy

Thrombolytic therapy has a direct lytic effect on the established thrombus, promoting dissolution of the thrombus and restoration of arterial patency. Thrombolytic drugs that have been used include streptokinase, urokinase and tissue plasminogen activator. The advantage of tissue plasminogen activator is that it is a more specific and/or targeted therapy, acting on cross-linked fibrin rather than circulating fibrinogen or plasminogen, reducing the risk of a systemic fibrinolytic state. However, although this approach would seem the more logical and effective treatment for ATE, it carries a high risk of severe reperfusion injury following recanalization of the occluded vessel, with associated high morbidity and mortality. In reported cases, thrombolytic therapy for ATE in cats was no better in terms of hospital discharge rate or survival than conservative treatment, and in some cases there were severe adverse effects (Killingsworth *et al*., 1986; Moore *et al*., 2000). Thrombolytic therapy is not recommended at the current time for feline ATE.

Supportive treatment

Supportive treatment is required to maintain body temperature, hydration status and nutritional status, as most cats are hypothermic, dehydrated and anorexic on presentation. Fluid therapy may also be required. This should be undertaken with extreme caution as these patients are very prone to fluid overload and may be easily pushed into CHF. Fluid therapy is contraindicated in patients with concurrent CHF. If azotaemia, dehydration and/or anorexia are a concern in patients with ATE and CHF, the initial diuretic dose administered should be low; it is not recommended to give diuretics and fluids concurrently.

If necessary, limbs may be bandaged to prevent self-mutilation of devitalized extremities. Limb viability should be monitored closely, and limb amputation or skin grafts may be required once the cat has been stabilized. Physiotherapy, including muscle massage and passive exercises, may stimulate motion and perfusion of the affected limbs.

Blood parameters (renal function, electrolyte status and ideally coagulation profiles) should be monitored closely. If a cat has an embolism within the renal artery, this will become evident on sequential monitoring. Vasodilator therapy (e.g. acepromazine, hydralazine) has been suggested to encourage opening of the collateral circulation; however, there is no proof of efficacy and it may exacerbate systemic hypotension, so is not recommended.

Reperfusion injury

Reperfusion injury typically occurs hours to days after the thromboembolic event and is caused by reperfusion of the damaged muscle tissue, which results in a sudden release of metabolic waste products into the systemic circulation. The marked increase in potassium and hydrogen ions may cause severe life-threatening hyperkalaemia and metabolic acidosis.

If a patient being treated for ATE suddenly becomes arrhythmic and/or bradycardic, an ECG should be performed and serum potassium levels measured. Typical ECG findings with severe hyperkalaemia include absence of P waves, widened QRS complexes (occasionally normal morphology is seen) and large and peaked T waves. These findings indicate atrial standstill (see Figure 6.26). Patients with hyperkalaemia are not always bradycardic, so a normal or even increased heart rate does not exclude severe hyperkalaemia.

This syndrome requires prompt intervention in an attempt to stabilize the heart rhythm and reduce serum potassium levels. Calcium gluconate (10% at a rate of 0.5–1.5 ml/kg slowly i.v. over 10–15 minutes) antagonizes the myocardial effects of hyperkalaemia and is the most efficient drug to address the cardiac arrhythmias. Continuous ECG monitoring is required during the administration of calcium gluconate. Administration should be interrupted if new arrhythmias develop. Hypertonic glucose (50% dextrose at a rate of 0.5–1.5 g/kg i.v. over 5 minutes) should be administered to decrease the serum potassium level. Alternatively, dextrose can be combined with insulin to promote faster entry of potassium into the cells (regular insulin at a dose of 0.1–0.5 IU/kg plus dextrose at a rate of 2 g/IU of insulin i.v.).

Prognosis

The short-term prognosis depends on the nature of the underlying cardiomyopathy and the response of CHF to treatment. Factors associated with a better prognosis are a single affected limb with some retained motor function, and the presence of normothermia. Factors associated with a poor prognosis are both hindlimbs affected with no motor function, the presence of CHF and hypothermia.

Rectal temperature is one of the best prognostic indicators of survival. Cats presenting with a rectal temperature below 37.2°C have a <50% probability of survival (Smith *et al*., 2003).

It can take up to 2 weeks for motor function to begin to return in limbs following resolution of a 'saddle' thrombus, and up to 6 weeks for motor function to return to normal. If the cat recovers, permanent limb damage is rare. As many as 75% of cats will experience recurrent ATE episodes within days to months of the initial episode, although some studies report survival for several years (Smith *et al*., 2003; Hogan *et al*., 2015).

Mortality and morbidity following recovery from an acute episode of ATE are more likely to be associated with progression of the underlying heart disease, rather than recurrent ATE (Smith *et al*., 2003). Conservative management and supportive care have been shown to be associated with a hospital discharge rate of approximately 50%, which reflects the poor outcome of ATE. Thus, the decision to treat a patient with ATE should be made following a thorough discussion with the owners and consideration of the different factors known to be associated with prognosis on an individual basis.

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Chapter 7

General approach to respiratory distress

Lori S. Waddell and Lesley G. King†

Diagnosis

Respiratory distress is caused by a low arterial partial pressure of oxygen (P_aO_2) (hypoxaemia), a high arterial partial pressure of carbon dioxide (P_aCO_2) (hypercapnia), or a significant increase in the work of breathing. Normally, ventilation is stimulated by increases in arterial carbon dioxide concentration, and decreased by hypocapnia. Hypoxia only acts as a respiratory stimulus if P_aO_2 falls below 50 mmHg, when hypoxic drive overrides the effects of hypocapnia that may be present due to hyperventilation.

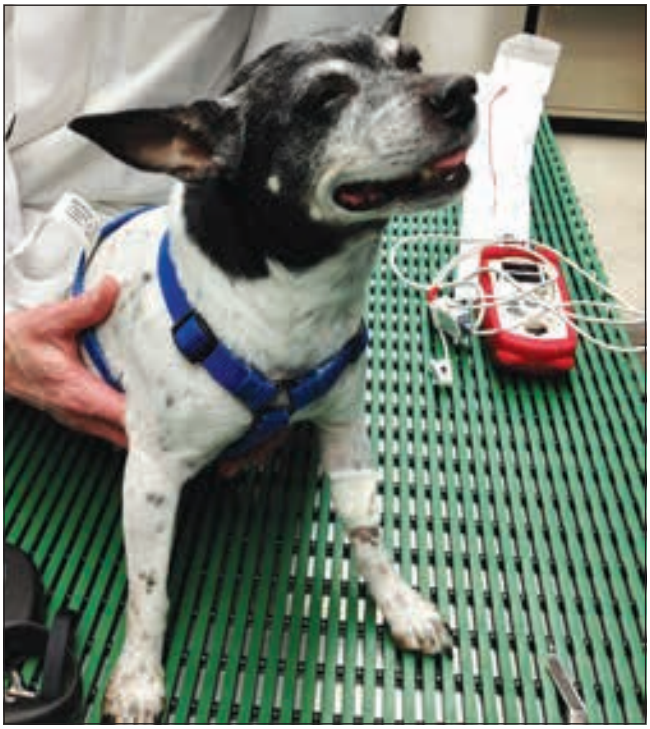
It is essential that patients in respiratory distress are recognized immediately. In the emergency room, observation of the patient and a detailed physical examination of the respiratory and cardiovascular systems are the most important tools for diagnosis and treatment, often providing clues about the causes of distress when more stressful diagnostic procedures are not possible. Based on the physical examination and a brief history, the clinician should attempt to localize the disease process to the airways (upper or lower), lungs or pleural space, facilitating immediate steps to stabilize the patient.

Observation of respiratory patterns

Dogs and cats in respiratory distress have an increased respiratory rate and effort. Increased respiratory effort is a sign of increased respiratory drive. This is manifested by recruitment of the secondary muscles of respiration, including the scalene and sternomastoid muscles of the neck and chest, the alae nasae, which dilate the nostrils, and the muscles of the abdominal wall, which contract when expiration becomes an active rather than a passive process. Recruitment of the secondary muscles of respiration is a non-specific response to increased respiratory drive, occurring in patients in respiratory distress but also in normal animals that are exercising, fearful or in pain.

In contrast, 'paradoxical respiration' is a manifestation of marked inspiratory effort that is only seen in animals with respiratory disease. Concurrent outward movement of both the chest and abdomen characterizes normal inspiration. Paradoxical respiration is recognized by a lack of synchronous movement of the chest and abdominal walls; the diaphragm and caudal intercostal and abdominal muscles tend to collapse inwards and forwards during inspiration. Unlike increased respiratory effort alone, paradoxical respiration is a specific indication of respiratory distress, increased work of breathing and the presence of respiratory muscle fatigue. It may also be seen less commonly in patients with abnormal diaphragmatic movement secondary to paralysis or rupture.

Postural adaptations are common in patients with respiratory distress, minimizing resistance to air flow. Many patients in severe respiratory distress breathe through an open mouth to remove the resistance to air flow produced by the nasal turbinates. Similarly, the neck is often extended and the head lifted to straighten the trachea. Most patients in respiratory distress demonstrate some degree of orthopnoea, preferring to stand or lie in sternal recumbency and abducting their elbows to minimize compression of the chest wall and to recruit the accessory muscles of ventilation, such as the latissimus dorsi (Figure 7.1). Any restraint that limits postural adaptations may lead to further hypoxaemia and decompensation, a fact that must be borne in mind when restraining these animals for diagnostic procedures such as radiography.

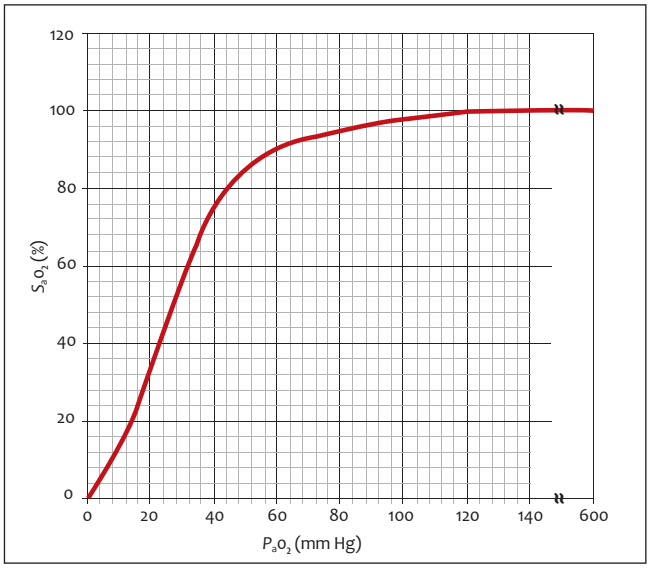


7.1 A terrier presented in severe respiratory distress. Note the open mouth, extended neck and abducted elbows.

Physical examination

Mucous membrane colour can yield important information about the functional status of the respiratory system. Due to the shape of the oxyhaemoglobin dissociation curve (Figure 7.2), cyanosis occurs only with severe hypoxaemia (<80% saturation of arterial blood); when moderate hypoxaemia is present, the mucous membranes may still be pink. Clinicians should therefore not be lulled into a false sense of security by pink mucous membranes. At least 50 g/l of desaturated haemoglobin must be present for the blue colour of cyanosis to be detectable. Thus, anaemia or peripheral vasoconstriction, which lead to pale mucous membranes, also lead to an inability to detect cyanosis. Cherry red or muddy chocolate mucous membranes are rarely detected but can indicate the presence of toxins such as cyanide and paracetamol (acetaminophen), respectively. Carbon monoxide can also cause bright red mucous membranes (carboxyhaemoglobin). These toxicities cause respiratory distress despite a normal P_aO_2 by interfering with haemoglobin binding and release of oxygen, or with the ability of the tissue to utilize oxygen.

A limited physical examination of the respiratory and cardiovascular systems can be performed rapidly and can be very rewarding. Auscultation of the chest and cervical trachea may detect wheezes, crackles, harshness or increased bronchovesicular sounds, as well as areas of dullness (dorsal, ventral, unilateral). A judgement should be made as to whether the sounds are louder or quieter than expected for the degree of respiratory effort the animal is showing. Wheezes are musical or squeaky sounds associated with narrowing of the airways secondary to inflammation, mucosal oedema, mucus or masses. If wheezes occur during inspiration, upper airway pathology should be suspected, whereas disease of the small bronchi or lower airways, such as feline allergic bronchitis, generally produces expiratory wheezes.



7.2 The oxyhaemoglobin dissociation curve demonstrates the relationship between partial pressure of oxygen dissolved in the blood (P_aO_2) and the saturation of haemoglobin with oxygen (S_aO_2). The sigmoid shape of the curve occurs as a result of a conformational change in the haemoglobin molecule following binding of the first molecule, allowing binding of the remaining three molecules to occur more rapidly. This facilitates both oxygen intake in the lungs and oxygen release to the tissues. The plateau of >90% haemoglobin saturation also provides a wide margin of safety – lung disease may result in significant decreases in P_aO_2 without a concurrent decrease in saturation. Desaturation can occur rapidly, however, once the P_aO_2 decreases to a value of <60 mmHg.

Crackles are discontinuous popping sounds that usually indicate the presence of fluid in the alveoli and airways. They are caused by air bubbling through fluid, but can also be caused by the opening and closing of small bronchi and alveoli. Soft end-inspiratory crackles occur with parenchymal disease and often indicate pulmonary oedema, haemorrhage or purulent exudate in the alveoli. Loud snapping airway crackles during inspiration can be heard in dogs with pulmonary fibrosis or chronic bronchitis. If the lung or heart sounds are dull, muffled or difficult to hear, pleural space disease should be considered. The most common pleural abnormalities include pneumothorax, pleural effusion, diaphragmatic hernia and neoplastic masses. In cats, diminished chest compressibility can suggest an effusion or mediastinal mass.

Auscultation of the heart and simultaneous palpation of the pulses help to determine whether cardiovascular disease is contributing to respiratory dysfunction. In dogs with congestive heart failure, a mitral murmur or supraventricular dysrhythmia (often atrial fibrillation) is usually detected. In the absence of these findings, heart failure as a cause of respiratory distress is extremely unusual. Use of auscultation to rule out cardiovascular disease may be more difficult in cats, as abnormal heart sounds and dysrhythmias may be absent or intermittent in cats with heart disease, even those with congestive heart failure (see Chapter 6). The presence of pulse deficits (auscultated heart sound without a concurrent pulse) strongly suggests the presence of an arrhythmia.

Emergency stabilization

Initial stabilization of patients with severe respiratory distress should include increasing the inspired oxygen concentration (oxygen therapy), while a rapid but thorough physical examination is performed. Ideally, the patient should be allowed to rest briefly in an oxygen-enriched environment before further diagnostic investigation and manipulation. This is particularly important for cats, as it allows calming and recovery from transport. A more complete examination and further investigations are performed only when tolerated and shown not to exacerbate signs of distress. An exception is made when dull lung sounds are auscultated, suggesting the presence of pleural space disease. In this situation, thoracocentesis should be attempted promptly, to remove pleural air or fluid (see below), even before radiographs are obtained. Patients in respiratory distress may not be stable enough for radiography or other diagnostic procedures, and thoracocentesis may be not only diagnostic but therapeutic.

Oxygen supplementation

Emergency oxygen therapy can be supplied in several ways, and should be provided to any patient that presents in even mild to moderate respiratory distress, as well as those that are in severe distress. There are minimal risks associated with oxygen supplementation and most patients will rapidly benefit from it. Mask oxygen can be used on any patient that is lying still and tolerates the mask. It may be poorly tolerated in distressed patients and persistent attempts to place the mask over the muzzle can increase stress. With a tight-fitting mask at high oxygen flow rates (5–6 l/min), a fractional inspired oxygen concentration (F_iO_2) of 0.7–0.8 can be achieved (room air F_iO_2 = 0.21). Care must be taken that the mask is not so tight as to cause rebreathing of carbon dioxide and consequent hypercarbia.

Flow-by oxygen is achieved by holding the oxygen supply tubing near the nostrils or mouth of the animal and provides a similar effect to a mask, with much less stress.

An oxygen pipe from an anaesthetic machine can supply oxygen (5–8 l/min) to an Elizabethan collar covered with clingfilm, leaving 2.5–5 cm open at the top of the collar to allow for carbon dioxide and water vapour to be eliminated. This technique allows the animal to be visible and minimizes stress, but is not tolerated by all patients. The humidity and temperature within the enclosed space of the Elizabethan collar may increase fairly rapidly, which can limit the duration for which this technique can be employed.

Oxygen cages are one of the easiest methods of oxygen administration, but they isolate the patient, making it difficult to examine, monitor and treat these dynamic cases (Figure 7.3). This may be an advantage in some stressed cats that may benefit from enforced isolation from strange people in a strange environment. Initial crisis management of animals in respiratory distress may require high oxygen concentrations (F_iO_2 up to 0.9) until the patient has been stabilized. Although it should be possible to reach an F_iO_2 of up to 1.0, some oxygen cages cannot raise the F_iO_2 above approximately 0.5, which may be too low for severely dyspnoeic animals. Opening the cage door drops the F_iO_2 to that of room air almost immediately. Oxygen cages may also be associated with inappropriate patient warming and consequent hyperthermia. Large dogs may not fit into standard oxygen cages. Despite these limitations, oxygen cages may represent a useful investment for the emergency practice. At present, no commercially available oxygen supplementation cages for large dogs are available in the UK, although they may be purchased from the USA. Paediatric incubators, into which oxygen is piped, provide a suitable alternative for cats, small dogs and neonates, attaining oxygen concentrations of 80–90%. These allow good observation of the patient and, although expensive when purchased new, are often available second-hand from human hospitals.

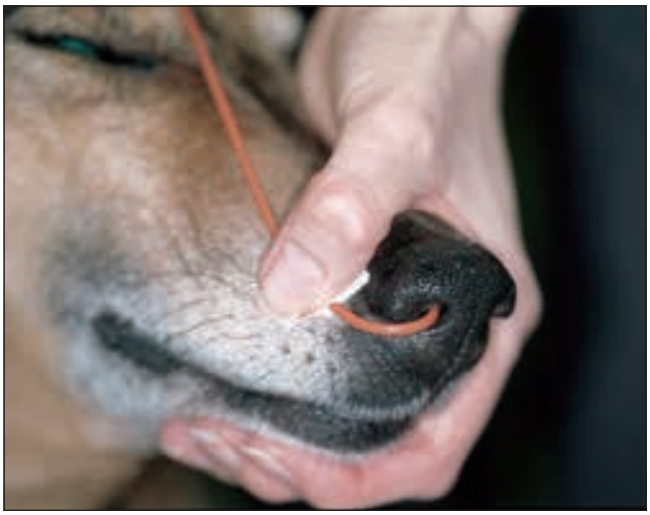
For more prolonged oxygen supplementation, nasal oxygen can be provided with nasal oxygen prongs that are manufactured for human patients (Figure 7.4), or by placing a catheter in one or both nostrils and suturing or gluing it in place (Figure 7.5). Nasal prongs penetrate approximately 1 cm into both nostrils and usually work well in large-breed dogs that are relatively immobile.



7.3 A Field Spaniel in congestive heart failure was placed in an oxygen cage to provide oxygen supplementation. He was in severe respiratory distress and would not tolerate an oxygen mask or nasal prongs. Temperature, inspired oxygen concentration and humidity can be controlled in these units.



7.4 Nasal oxygen prongs that are manufactured for human patients can be used in many canine patients to provide oxygen supplementation.



7.5 Nasal oxygen can also be provided by suturing a red rubber catheter into one nostril and inserting it a premeasured length equal to the distance from the nostril to the medial canthus of the eye.

Nasal catheters can be used in dogs or cats of almost any size. Any type of catheter can be used for this purpose; most commonly 5–8 Fr red rubber urinary catheters or soft feeding tubes are used (Figure 7.6). Brachycephalic breeds are poor candidates for nasal oxygen supplementation: catheter prongs cannot be adjusted to fit comfortably on their faces; nasal catheters may not fit due to stenotic nares or do not stay in place because their noses are short; and increased vagal tone may be aggravated by the nasal catheter. Animals that are mouth breathing are also poor candidates for this technique, as increased air mixing in the pharynx leads to a reduced effective F_iO_2. Generally, nasal oxygen is thought to give an F_iO_2 of approximately 0.4 depending on the flow rate of oxygen, the size of the animal and its minute ventilation. The F_iO_2 can be increased by placement of a second nasal catheter in the other nostril.

Alternatively, a long intravenous catheter can be placed percutaneously into the trachea following the instillation of surface local anaesthetic. Humidified oxygen is supplied at similar flow rates to those used with the nasal catheter. This system may be especially useful in individuals with laryngeal or upper tracheal obstruction.

- Used to provide supplemental oxygen in patients that are not tolerating nasal prongs and are too large to fit into an oxygen cage or if an oxygen cage is not available.
- Red rubber catheter/soft feeding tube, usually 8 Fr (or 5 Fr in small dogs) is used
  1. The distance from the nose to the medial canthus of the eye is measured and marked on the catheter.
  2. The nostril is numbed with topical anaesthetic such as lidocaine gel or one to two drops of 2% lidocaine dripped into the nostril.
  3. The catheter is inserted through the nostril into the ventral meatus to the premeasured distance.
  4. The catheter is sutured in place using 2 metric (3/0 USP) nylon and tape butterflies, just beside the nostril and again on the side of the face or on top of the head.
- Single or bilateral nasal catheters can be used depending on the percentage of oxygen supplementation that is required
- An Elizabethan collar may be necessary to prevent the patient from removing the catheter. Complications may include excessive sneezing, dislodgement, epistaxis or increased dyspnoea if upper airway disease is present

7.6 Nasal oxygen catheter.

If it is provided for more than a few hours, oxygen should be humidified (saturated with water vapour) to prevent desiccation of the airways, especially if the turbinates are bypassed, as occurs with nasal or tracheal oxygen catheters. Specially designed units that heat and humidify the inspired air are available for placement in anaesthetic and ventilator circuits, but nasal or cage oxygen humidification can be simply accomplished by bubbling the oxygen through a chamber of distilled water (Figure 7.7).

Long-term therapy with high concentrations of oxygen (F_iO_2 >0.6 for more than 12 hours) is associated with damage to the lung called oxygen toxicity. Inflammatory injury is caused by toxic metabolites of oxygen, including oxygen free radicals and superoxide molecules. Clinically, oxygen toxicity is difficult to diagnose, but changes in the lungs are similar to those seen in the acute respiratory distress syndrome (ARDS). Every effort should be made to minimize the F_iO_2 used to maintain critical patients. In the presence of severe respiratory distress, however, it may not be possible to decrease the F_iO_2 without provoking severe distress, and the clinician may have to accept the risk of oxygen toxicity in the interests of survival of the patient.



7.7 Oxygen can be humidified by bubbling it through a chamber filled with distilled water. This reduces airway irritation by preventing desiccation.

Intravenous access

Intravenous access with an indwelling peripheral catheter placed in the cephalic or saphenous vein should be obtained early during the hospitalization of all patients with respiratory distress. The catheter should be placed with minimal restraint and stress. Establishment of intravenous access allows administration of drugs and, if the animal decompensates, provides a means to administer intravenous anaesthesia to facilitate rapid control over the airway.

Thoracic ultrasonography

Thoracic ultrasonography can be very useful for confirming the presence of pleural effusion or soft tissue (mass, herniation of abdominal organs) in the pleural space. It is a rapid, relatively non-stressful diagnostic tool that can also aid in performing thoracocentesis by identifying areas with the greatest volume of fluid accumulation and structures that need to be avoided. In many patients, it is a much quicker and less stressful procedure than thoracic radiography, especially since the patient can remain in sternal recumbency. The tFAST (thoracic focused assessment with sonography for trauma) technique can be used to assess for the presence of pneumothorax or pleural effusion. Pneumothorax is diagnosed by the absence of the 'glide sign', defined as lack of the normal dynamic interface between the lung margins and thoracic wall during respiration. Concurrent thoracic trauma can be diagnosed by the presence of pleural or pericardial fluid or the presence of a 'step sign', defined as an abnormal glide sign. A step sign is a glide sign that deviates from the normal linear continuity of the pulmonary–pleural interface and is assumed to represent thoracic injury.

Thoracic radiography

Thoracic radiography represents one of the most useful diagnostic tools for the clinician faced with a patient in respiratory distress. Detailed information about thoracic radiography is available in Chapter 24. Although valuable information is often provided, radiography is a stressful procedure that can cause significant respiratory decompensation and it is generally not advisable in patients in severe respiratory distress. To minimize stress, dorsoventral radiographs can be obtained with the patient restrained in sternal recumbency. Although this view provides less useful diagnostic information and care must be taken not to over-interpret the image, it is also less likely to compromise ventilatory function. Alternatively, horizontal beam lateral views may be obtained where possible. The animal should be measured and radiograph settings calculated in advance of moving and positioning the patient for radiography. Supplementation of inspired oxygen should be continued during the procedure. If the animal can tolerate the manipulation, it is ideal to obtain at least two and ideally three views of the thorax.

Approach to undiagnosed respiratory distress

When the initial history does not provide specific useful information, the approach to the patient in respiratory distress is to treat according to the apparent site of respiratory pathology. The history, signalment and physical

examination are often sufficient to determine which areas of the respiratory system are involved. For this purpose, the respiratory tract is divided into the airways (upper and lower), the pulmonary parenchyma, and the pleural space and thoracic cage. After determining which of these anatomical areas is affected, a list of differential diagnoses, diagnostic procedures and therapeutic strategies is then formed for the individual patient.

Upper airway disease

Clinical signs

The clinical signs of disease of the upper airway are listed in Figure 7.8. Upper airway disorders almost always cause loud noises that are audible without a stethoscope. On auscultation, upper airway noise is loudest over the trachea. Referred sounds may also be heard on auscultation of the lungs. Most dogs with dynamic upper airway obstructions (such as brachycephalic obstructive airway syndrome (BOAS) or laryngeal paralysis) have stridor or stertor, primarily on inspiration. Negative inspiratory pressure tends to close the upper airway, whereas during expiration the airway opens. Animals with fixed upper airway obstructions (such as masses or abscesses) tend to have difficulty during both inspiration and expiration.

Differential diagnosis of upper airway obstruction

- Brachycephalic obstructive airway syndrome
- Laryngeal paralysis
- Tracheal collapse
- Nasopharyngeal polyps (cats)
- Aspirated foreign bodies
- Upper airway neoplasia
- Retropharyngeal masses, abscesses or haematomas

Clinical and historical signs associated with upper airway obstruction

- Dyspnoea
- Audible stridor or stertor
- Increased respiratory effort with prolonged inspiratory time (gasping respiration)
- Change in vocalization (bark or meow)
- Exercise intolerance – clinical signs most severe when stressed or exercising
- Excessive panting
- Hyperthermia

7.8 Common differential diagnoses and clinical and historical signs associated with upper airway or laryngeal obstruction in dogs and cats.

Respiratory distress in animals with upper airway obstruction is made worse by exercise or excitement, and is reduced or almost absent at rest. Increased respiratory drive results in enhanced negative inspiratory pressures during exercise, leading to more severe narrowing of the airway. Tests of pulmonary function during dyspnoeic episodes often reveal significant hypoxia and hypercarbia, whereas these parameters may become almost normal at rest. This return of pulmonary function to normal at rest is one of the hallmark signs of upper airway obstruction; blood gases usually remain abnormal at rest in animals with parenchymal or pleural disease.

Many dogs with upper airway obstruction suffer from concurrent hyperthermia. They are unable to thermoregulate effectively because an insufficient volume of air passes over the tongue during panting. Hyperthermia starts a vicious cycle, as it stimulates an increased respiration rate and panting, which further narrows the airway.

General approach to management of patients with upper airway obstruction

Management of animals with upper airway obstruction is summarized in Figure 7.9. The most important priority is to encourage the animal to rest quietly in an oxygen-enriched environment. Many benefit considerably from sedation; acepromazine is the drug of choice provided that the animal is not hypovolaemic (phenothiazines may be associated with vasodilation, which exacerbates signs of hypovolaemia) or brachycephalic (brachycephalic breeds may have increased sensitivity to phenothiazines and therefore a lower dose should be used). The dose of acepromazine should be kept to a minimum and may be more effective if combined with an opioid (neuroleptanalgesia). Opioids may also be used alone if there is hypovolaemia, as these agents produce minimal cardiovascular effects. Suggested agents include morphine, methadone, oxymorphone (USA) or butorphanol, any of which may be combined with a sedative such as diazepam if they trigger excessive panting.

- Oxygen supplementation: oxygen cage best
- Rest, sedation if necessary
- Acepromazine at 0.001-0.005 mg/kg i.v. or i.m. if cardiovascularly stable
- If collapsed or sedated, extend head and neck and pull tongue out of the mouth
- Vascular access
- Minimal stress
- Anti-inflammatory dose of corticosteroids (dexamethasone at 0.1–0.2 mg/kg i.v. or i.m.
- Monitor temperature, vigorous efforts to cool if needed
- Fluid therapy if dehydrated or hypovolaemic
- Emergency tracheostomy or intubation if no response to medical management

7.9 Management of patients with upper airway obstruction.

Manipulation and stress should be kept to a minimum, but if the animal is collapsed or sedated, the head and neck should be extended and the mouth opened with the tongue pulled forward to minimize airway resistance. Corticosteroids at anti-inflammatory doses are often very helpful if significant airway oedema or inflammation is present. They should be avoided initially if neoplasia is one of the differential diagnoses. Corticosteroids may cause lysis of malignant lymphocytes, thereby making it difficult to confirm the diagnosis. Core body temperature should be monitored carefully and vigorous attempts made to cool the patient with fans (after wetting the fur) or cool intravenous fluids if the temperature is >39°C.

Animals that do not respond to this approach should be anaesthetized and intubated, or a tracheostomy performed if necessary (Figures 7.10 and 7.11). Ideally, these animals should not remain intubated through the larynx for more than a few hours, as the tube triggers swelling that may exacerbate the problem following extubation.

In many syndromes of upper airway obstruction, pharyngoscopy and laryngoscopy under general anaesthesia are required to confirm the diagnosis. Following this, steps should be taken to relieve the airway obstruction prior to anaesthetic recovery. Attempts to recover patients without correcting the airway problem can be difficult and re-intubation may be necessary. If the underlying disease cannot be corrected immediately and the patient cannot be successfully extubated, a tracheostomy will be necessary. In less severe cases, particularly those with a dynamic airway obstruction, a slow, non-stressful recovery may be successful, allowing definitive surgical correction of the airway problem to be planned in the near future.

1. The patient should be anaesthetized and an endotracheal tube placed. Depending on the nature of the upper airway disease, the size of the endotracheal tube may be significantly smaller than is expected for the size of the patient.
2. Place the patient in dorsal recumbency, with the neck extended. A sand bag placed beneath the neck will help with positioning. The ventral cervical region should be clipped and aseptically prepared if time permits.
3. A ventral cervical midline incision is made from the caudal aspect of the cricoid cartilage to the sixth tracheal ring.
4. The sternohyoid muscles are separated on the midline and retracted laterally.
5. The trachea should be isolated and a full-thickness stab incision should be made through the annular ligament between the third and fourth tracheal rings.
6. The incision in the trachea is extended laterally so that approximately 50–60% of the tracheal circumference is incised.
7. A tracheostomy tube approximately 50% of the tracheal diameter is placed into the lumen. The endotracheal tube must be withdrawn immediately prior to tracheostomy tube insertion.
8. Two stay sutures are placed in the rings adjacent to the tracheostomy site to facilitate exposure for placement of the tracheostomy tube.
9. The subcutaneous tissues and skin are apposed cranial and caudal to the tracheostomy site allowing a large enough opening for re-intubation if necessary. The tube is then secured with umbilical tape tied around the neck.

- Patients with a temporary tracheostomy require careful 24-hour monitoring due to the risk of tube occlusion or dislodgement. Sterile technique should be used when handling the site, tracheostomy tubes and suction catheters
- Postoperative care includes nebulization of the tube site to humidify the airways, frequent removal and cleaning of the inner cannula (if present) to prevent obstruction with mucus, and observation for swelling and irritation. Regular suctioning of the airway is no longer recommended
- Short-term complications can include haemorrhage, obstruction of the tube, dislodgement, infection and damage to the peritracheal structures

7.10 Emergency tracheostomy.



7.11 A tracheostomy was created in this mixed breed dog for recovery from anaesthesia after surgery to correct laryngeal scarring. A 50% circumferential incision was made into the trachea between rings to place the tracheostomy tube. Stay sutures placed around the tracheal rings cranial and caudal to the incision can be seen.

Syndromes of upper airway obstruction

Brachycephalic obstructive airway syndrome: This is a common cause of respiratory distress in affected breeds such as English and French Bulldogs, Boston Terriers, Boxers, Pekingese and Pugs. The primary components of this syndrome are stenotic nares, redundant pharyngeal soft tissue, excessively long soft palate and hypoplastic trachea. Chronic obstruction of the upper airway causes increased negative inspiratory pressure, leading to further airway occlusion, inflammation and oedema of the redundant tissue, eversion of the laryngeal saccules and eventually, in end-stage cases, complete laryngeal collapse. In patients with BOAS, mouth breathing often improves the clinical signs because some of the airway resistance caused by the stenotic nares is eliminated. These animals often present with hyperthermia and acute respiratory distress during hot humid weather, after exercise, or when excited. Questioning the owners often reveals a history of chronic airway obstruction (snoring and airway noise), which the owners may interpret as 'normal for the breed'.

Initial treatment is as described above, including oxygen supplementation, sedation, cooling and corticosteroids. Most patients can be managed medically through the presenting crisis, but surgical intervention to prevent future episodes is strongly recommended. Surgical correction of the stenotic nares, everted laryngeal saccules (if present) and the over-long soft palate can greatly improve these patients, especially if performed in young dogs (<2 years of age).

Laryngeal paralysis: Laryngeal paralysis occurs in dogs and cats due to disruption of innervation of the muscles of the larynx and is classified as either congenital or acquired (idiopathic, traumatic, polyneuropathic or iatrogenic). Idiopathic acquired laryngeal paralysis is the most common form and is often seen in large-breed dogs such as Labrador Retrievers, Golden Retrievers and St Bernards. Affected dogs can present in severe respiratory distress with cyanosis and collapse. They often have loud inspiratory stridor and may be hyperthermic. The history may include voice change, gagging while eating and drinking, progressive exercise intolerance, and noisy breathing.

Immediate therapy is as described above, with severely affected animals requiring intubation or a temporary tracheostomy. Thoracic radiography should be performed, as concurrent aspiration pneumonia and non-cardiogenic pulmonary oedema are common. Definitive diagnosis is made by laryngeal examination on induction of anaesthesia, to determine whether the vocal folds abduct effectively and symmetrically during inspiration. Since anaesthesia affects movement of the larynx, anaesthesia must be light enough that the patient is almost coughing during the laryngeal examination. Paradoxical laryngeal motion is another source of error of interpretation during laryngoscopy. If the larynx is paralysed, inspiration may be

accompanied by closure of the larynx because of negative inspiratory pressures, and exhalation may tend to 'blow the larynx open'. This creates a paradoxical motion of the larynx, which on casual inspection may simulate normal function. Therefore, while performing a laryngeal examination, any observed movement of the larynx must be carefully correlated with the phase of respiration.

Surgical intervention may be delayed until the respiratory crisis has passed, allowing resolution of laryngeal inflammation and oedema. The surgical method of choice is a laryngeal tie-back (arytenoid cartilage lateralization). Postoperative concerns include aspiration pneumonia, laryngeal inflammation and oedema, haemorrhage and breakdown of the surgical repair. Postoperative complications can be minimized by keeping the animal as calm as possible and reducing vocalization or coughing in the first 24 hours after surgery.

Tracheal collapse: This is a common problem in middle-aged to older small-breed dogs with a progressive history of cough and exercise intolerance. A cough is usually easy to induce on tracheal palpation. Excitement often triggers a paroxysmal 'honking' cough and dyspnoea. The tracheal rings in these animals are often abnormally C-shaped and fibrodysplastic, and the dorsal tracheal membrane is stretched, floppy and weak. Obstruction of the tracheal lumen occurs in the cervical and/or thoracic trachea. Compression, elevation and collapse of the left mainstem bronchus may mimic the clinical signs of a collapsing trachea in dogs with mitral regurgitation and enlargement of the left atrium, before congestive heart failure occurs. Coughing due to mainstem bronchus compression is medically managed in a similar way to tracheal collapse, in addition to concurrent management of the primary cardiac disease.

Animals with tracheal collapse can present with varying degrees of respiratory distress. In the most severe cases, complete collapse of sections of the trachea can cause upper airway obstruction. Hypoxaemia can also occur during spasms of paroxysmal coughing. The diagnosis can be suggested using plain thoracic radiography. Severe collapse can appear radiographically similar to a tracheal soft tissue mass. One method of confirming the clinical diagnosis is observation of the trachea while coughing under fluoroscopy. The gold standard for diagnosis is bronchoscopy, but this requires anaesthesia, recovery from which is associated with a high degree of risk in severely affected patients if surgical correction is not performed at the time of diagnosis.

Management includes anti-inflammatory drugs and cough suppressants. Opioids, especially butorphanol and hydrocodone where available are antitussive at low doses and are often beneficial. If medical management is in-effective, surgical placement of extraluminal rings for patients with extrathoracic or thoracic inlet collapse or non-surgical placement of intraluminal stents for intrathoracic collapse may produce good results, even in patients with end-stage disease. Tracheostomy is usually not of benefit in these patients because the collapse typically occurs throughout the cervical region and intrathoracic trachea or mainstem bronchi.

Inflammatory nasopharyngeal polyps: These occasionally cause respiratory distress in young, otherwise healthy cats. Polyps are often associated with inflammatory disease of the tympanic bullae or auditory canals. These cats may have inspiratory stridor, a nasal discharge and otitis externa. Polyps are occasionally visible on oral examination in awake patients, but sedation is usually required for adequate visualization. The soft palate should be palpated and retracted to detect polyps in the nasopharynx, and a thorough otoscopic examination should be performed. Radiographs of the skull, bullae and nasal cavity should be obtained. Polyps may arise from the bullae, ear canals or nasopharyngeal mucosa and must be removed surgically. If there is evidence of otitis, bulla osteotomy may be considered to resolve the underlying cause of the polyp. If the entire polyp is removed, surgery is generally curative.

Aspirated foreign bodies: These can cause sudden onset of respiratory distress if the foreign body obstructs the airway. Large upper airway obstructions require immediate action, since they may completely block all air flow. The animals often panic and are difficult to restrain, and sedation or anaesthesia may be necessary. If possible, vascular access should be established to allow intravenous administration of anaesthetic drugs. As it may be impossible to remove the foreign body fast enough, preparation for an emergency tracheostomy is prudent. After expeditious removal of the object, supplemental oxygen should be administered. If the animal is unconscious after foreign body removal, it should be intubated and ventilation assisted until spontaneous breathing and consciousness return.

Upper airway masses: Upper airway neoplasia can cause upper airway obstruction. Neoplasia usually causes a slow onset of respiratory distress unless the tumour is very rapidly growing or associated with an abscess. Lymphoma is the most commonly observed neoplasm, especially in cats, but any oral, laryngeal or tracheal neoplasm may be involved (Figure 7.12). Oxygen supplementation and sedation may be sufficient to improve clinical signs if the animal is not too severely affected. If necessary, when the neoplasm is in the proximal trachea or above, emergency tracheostomy can provide an adequate airway until more definitive surgery is performed. If the neoplasm is in the thoracic trachea and the patient cannot be stabilized medically, intubation (if possible), thoracotomy or palliative placement of an intraluminal stent are the only options.



7.12 Right lateral cervical radiograph of a 9-year-old male neutered Domestic Shorthair cat that presented with a 2–3-week history of decreased appetite, 3-day history of anorexia and increased upper airway noise with respiratory distress. Note the large laryngeal mass.

Retropharyngeal masses, abscesses and haematomas are an occasional cause of respiratory distress. The most common retropharyngeal neoplasm is lymphoma, while abscesses can result from haematogenous spread or foreign body penetration. Rapid diagnosis by pharyngoscopy, ultrasonography, advanced imaging techniques such as computed tomography (CT) or magnetic resonance imaging (MRI), fine-needle aspiration (FNA) or even exploratory surgery is essential. These animals can easily progress to complete obstruction of the airway and may require emergency tracheostomy. Haematomas can occur secondary to anticoagulant rodenticide ingestion, *Angiostrongylus vasorum* infection or trauma. In animals with coagulopathies, FNA and surgery are contraindicated. Haemostasis can be difficult to achieve, but plasma transfusions and specific antidotes such as vitamin K1 should eventually lead to cessation of haemorrhage.

Feline viral upper respiratory tract disease: Viral upper respiratory disease is a common cause of nasal and ocular discharge, sneezing, fever and debilitation in cats. Feline calicivirus and feline herpesvirus (feline rhinotracheitis) are the most common viruses involved. Following exposure, there is an incubation period of 2–5 days. Calicivirus infection usually manifests as an acute onset of lethargy and fever, typically followed by mild hypersalivation, sneezing, conjunctivitis and oculonasal discharge. Ulcers are often evident on the tongue and soft palate. The cat usually recovers in 7–10 days. In contrast, feline herpesvirus often causes more severe illness with fever, profound serous to mucopurulent oculonasal discharge and excessive salivation. Respiratory distress and open-mouth breathing may occur because of nasal obstruction or viral pneumonia. Clinical signs usually resolve in 2–3 weeks, although in some cases nasal turbinate damage can be so severe that the cat is prone to bacterial upper respiratory tract infections over a prolonged period of time. Following recovery from acute infection with herpesvirus, clinically normal cats may remain persistently infected and act as carriers that continuously or intermittently shed virus.

Most cats with an acute viral upper respiratory infection respond well to supportive care and antibiotic therapy to treat secondary bacterial infections. In cats with dyspnoea, severe oral ulceration or difficulty swallowing, broad-spectrum antibiotic therapy may need to be administered parenterally rather than orally. Nutritional support is important; food may need to be heated in order to increase its palatability, and some severely affected cats may require tube feeding (see Chapter 22). Nursing care should include careful cleaning of discharges from the face. Antiviral drugs are usually unnecessary. Minimal data are available regarding the use of non-specific immune stimulants such as feline interferon. Numerous vaccines are available and are routinely used as part of the feline annual vaccination strategy, but are not recommended in cats that are already showing clinical signs. Although most vaccines reduce clinical signs of disease, they do not prevent infection and the subsequent development of a carrier state.

Infectious tracheobronchitis ('kennel cough'): Kennel cough is a syndrome of acute infectious tracheobronchitis in dogs, caused by infection with a number of different organisms, of which the most clinically important is *Bordetella bronchiseptica*. Other bacteria, such as *Streptococcus*, *Staphylococcus* and *Klebsiella* spp., have also been implicated. The most common viruses involved include canine parainfluenza virus, canine adenovirus-1 and -2, canine distemper virus, canine influenza virus, canine herpesvirus and reoviruses-1, -2 and -3. The typical history involves exposure to a coughing dog. After an incubation period of 2–7 days, affected dogs develop an acute hacking cough. Although the cough can be distressing to the owner, these dogs are often otherwise systemically healthy, active, eating normally and afebrile. In dogs with an acute onset of cough associated with concurrent fever, dyspnoea, systemic illness or depression, alternative diagnoses (including pneumonia secondary to viruses and/or *B. bronchiseptica*) should be considered.

B. bronchiseptica is specially adapted to infect the ciliated epithelium of the upper respiratory tract, attaching via fimbriae to the cilia of the mucociliary escalator. It secretes exotoxins that cause paralysis of the cilia, thereby eliminating one of the most important lung defence mechanisms, allowing the organism to persist in the airway for a prolonged period of time. Infectious tracheobronchitis is associated with acute inflammation of the upper airways and increased production of thick, viscous mucus.

Antibiotics used to treat infectious tracheobronchitis should be effective against *B. bronchiseptica* and should achieve adequate penetration through the blood–bronchus barrier into the mucus lining the bronchi. In adult dogs, good choices include doxycycline or fluoroquinolones. In puppies, azithromycin or doxycycline should be considered. Antitussive, expectorant and anti-inflammatory drugs may also contribute to the comfort of the patient and the client. Corticosteroids should be used with caution because of the infectious nature of the disease.

Parenteral and nasal vaccines are available for prevention of infection but are typically not used in animals already showing clinical signs. Vaccines may not completely prevent clinical illness; however, the severity of disease is likely to be considerably less in vaccinated dogs. Vaccines should be administered prior to anticipated exposure (e.g. prior to admittance to a boarding kennel).

Smoke inhalation: Animals that present after exposure to smoke from house fires can have varying degrees of respiratory difficulty. Damage is caused by direct thermal injury and by inhalation of noxious substances produced by combustion. The gases produced in the largest concentration during combustion are carbon monoxide, hydrogen cyanide and carbon dioxide. All three of these gases, combined with low concentrations of oxygen, can cause narcosis. They combine very rapidly with haemoglobin, diminishing its availability and effectiveness for oxygen transfer. Animals that have been exposed to smoke in fires should be treated immediately with a high inspired concentration of oxygen to attempt to displace these gases from haemoglobin. Oxygen therapy should be continued for at least an hour. Other gases produced by combustion vary depending on the materials that have burnt and some can be extremely toxic.

The upper airway can become obstructed by inflammation and oedema from thermal burns. Patients should be monitored for signs of laryngeal or upper airway obstruction, and tracheostomy or intubation performed if necessary. Airway damage often includes severe necrotizing tracheobronchitis, which is accompanied by exudate and cough. Bacterial pneumonia can follow due to damaged lung defences and proliferation of bacterial pathogens. In worst-case scenarios, diffuse inflammatory damage to the lung may be recognized, manifesting as generalized acute lung injury (ALI) that can progress to ARDS.

Treatment of smoke inhalation should consist of oxygen supplementation, saline nebulization and coupage to promote clearance of material from the airways, bronchodilators and supportive care. Corticosteroids are not recommended in these patients because they are already locally immunosuppressed from the thermal damage to the respiratory tract. Prophylactic antibiotics should be avoided, as their use prior to the development of pneumonia will only select for resistant bacteria. As with all patients at risk for pneumonia, careful monitoring for clinical signs should be followed by a tracheal wash for cytology, culture and sensitivity testing before initiating antibiotic therapy.

Lower airway disease

Clinical signs

Clinical signs of animals with lower airway disease are summarized in Figure 7.13. Disease of the lower airways usually refers to abnormalities of the small bronchi and is commonly inflammatory in origin. Coughing is the most common historical finding. Typically, the cough is harsh or honking and non-productive. This type of cough is not beneficial to the patient, as it tends to exacerbate inflammation, thereby promoting further coughing. In contrast, animals with productive coughing (usually a soft moist sound that is followed by swallowing when the animal expectorates material into the pharynx) should be evaluated for other disorders such as pneumonia. In pneumonia, the cough is a necessary part of the clearance mechanism of the lung rather than being due to bronchial disease alone. On auscultation, most dogs with lower airway disease have increased bronchovesicular sounds and/or wheezes. Patients with end-stage disease may have significantly increased respiratory rate and effort associated with hypoxia. Thoracic radiographs reveal minimal evidence of alveolar disease.

- Cough
- Exercise intolerance
- Dyspnoea (severe cases, expiratory dyspnoea in cats with feline asthma)
- Increased bronchovesicular sounds
- Wheezes on auscultation

7.13 Clinical and historical signs associated with lower airway (bronchial) disease in dogs and cats.

Hypoxia in animals with chronic bronchitis is thought to be attributable to inequality of ventilation and pulmonary perfusion (V/Q mismatch) mainly caused by bronchial obstruction. Bronchial obstruction follows increased mucus production, mucosal hyperaemia and oedema, as well as early collapse of abnormal and weakened small airways. Obesity often contributes to the severity of the clinical signs, causing diminished ability to expand the lungs because of pressure on the thorax from the chest wall and abdomen. Bronchopneumonia is a common complication because of diminished lung defences. Although some degree of bronchoconstriction can occur, dogs do not suffer from smooth muscle spasm as seen in cats with feline allergic airway disease (asthma). Acute severe bronchoconstriction in cats with hyper-responsive airways contributes significantly to respiratory distress in affected animals. Animals with severe lower airway disease therefore present with respiratory distress caused by end-stage chronic obstructive pulmonary disease, superimposed bronchopneumonia and, in cats, bronchospasm.

General approach to management of patients with lower airway disease

Priorities for management of lower airway disease in dogs and cats are summarized in Figure 7.14. Animals brought to the emergency room because of lower airway disease are usually presented during exacerbations and crises, or when the disease has become end stage. Respiratory distress is a common presentation, especially in cats with asthma. Oxygen supplementation is the first priority. Animals that are extremely distressed may also benefit from sedation. Early diagnostic investigation should include thoracic radiography once the patient has been stabilized. Most patients with bronchial disease have little or no alveolar disease visible on thoracic radiographs. A peribronchial pattern may be present, with 'doughnuts' and 'tramlines', but alveolar disease should be absent unless pneumonia or another secondary process is present. Cats with bronchial disease often have lung hyperinflation, radiographically identified by a flattened diaphragm and evidence of air-filled lung between the caudal border of the heart and the diaphragm.

- Oxygen supplementation
- Rest; sedation not usually required
- Minimal stress
- Vascular access
- Anti-inflammatory doses of corticosteroids (not immunosuppresive)
  - Dexamethasone at 0.1–0.2 mg/kg i.v., i.m. q12h *or*
  - Prednisolone at 0.5–1 mg/kg i.v., i.m., orally q12h
- Bronchodilators
  - Terbutaline at 0.01 mg/kg i.v., i.m. q6–8h *or*
  - Aminophylline at 5.5 mg/kg i.v. q8h
- Cough suppressants
  - Butorphanol at 0.2–0.4 mg/kg i.v., i.m. *or* 0.5–1.0 mg/kg orally q6–12h *or* hydrocodone at 1.25–5 mg/kg orally q6–12h
- Antibiotics if there is evidence of concurrent pneumonia
- Thoracic radiographs to rule out pulmonary alveolar disease
- Consider tracheal wash (see Figures 7.15 and 7.16) for culture and cytological examination

7.14 General approach to emergency management of dogs and cats with lower airway disease.

If bronchial disease is suspected, corticosteroids can be extremely helpful because of the role of inflammation in the disease process. Initially, high doses are indicated, but should be reduced to the minimal effective dose as soon as possible. Bronchodilators such as terbutaline and aminophylline are also considered first-line drugs in these patients. Both corticosteroids and bronchodilators are typically administered by the intravenous or intramuscular route. The administration of bronchodilators and corticosteroids by aerosolization can be helpful but may not be tolerated by extremely dyspnoeic animals, and should supplement, rather than replace, parenteral drug administration in an emergency situation. Administration by the aerosol route is likely to be most useful in patients that are already accustomed to this route of administration as part of a chronic management plan. Refractory coughing may respond to antitussive drugs such as butorphanol. Mild sedation may also be beneficial, with low doses of acepromazine being effective in many patients. Since exacerbation of the clinical signs may occur due to secondary bacterial infection and even pneumonia, antibiotics may be of value in some cases to diminish exudate production. Ideally, cytology and culture of samples obtained from the airway (usually obtained by tracheal wash; Figures 7.15 and 7.16) should be undertaken prior to starting antibiotic therapy. Most respiratory crises caused by bronchial disease respond well to medical management, minimal stress and an oxygen-enriched environment.

Trans-tracheal wash

- Used in medium to large-sized dogs
- A trans-tracheal wash can usually be performed without sedation unless the dog is fractious. Ideally, the animal should be alert enough to cough to aid in sample collection. An 18 G through-the-needle catheter is used to collect the sample: 20 cm length in smaller dogs; 30 cm length in larger dogs

1. The skin of the ventral neck from the larynx to the mid-trachea should be clipped and aseptically prepared.
2. A local anaesthetic such as lidocaine is infiltrated to the level of the trachea at the site of planned catheter placement. The site of insertion is typically between two and five tracheal rings distal to the larynx; precise counting of tracheal rings is not necessary.
3. The catheter is pushed through the skin. The trachea is isolated and stabilized between the thumb and forefinger, and the tip of the catheter is placed against the trachea between two rings. The tip of the catheter is held perpendicular to the trachea with the bevel of the needle facing down, and is 'popped' into the lumen of the trachea.
4. The needle is then angled downward and the entire length of the catheter is fed down the trachea.
5. If the catheter does not feed easily, the needle is backed out of the trachea about 0.25 cm as the tip of the needle may be pressed up against the back wall of the trachea, and the catheter is again fed into the trachea.
6. Once the full length of the catheter is in the trachea, the needle is withdrawn, the needle guard is placed around the needle and the stylet is removed from the catheter.
7. Approximately 5–10 ml of sterile saline is injected into the catheter.
8. Coupage is performed on the dog's chest to encourage coughing and productive sampling.
9. This injection procedure can be repeated up to three times if necessary to obtain an adequate sample. Only a small proportion of the instilled fluid will be recovered.
10. The sample is submitted in a sterile container for culture and cytology.
11. The catheter is removed from the dog's neck and a gauze square is placed over the entry point to stop any minor bleeding.

Alternatively, if a long through-the-needle catheter is not available, a standard over-the-needle catheter may be used. The catheter is placed in the trachea as described above and the stylet removed. A long male dog urinary catheter is then threaded through the intravenous catheter to approximately the level of the carina. This can be estimated by premeasuring the catheter to the 4th intercostal space. The saline is instilled through the urinary catheter. Typically a 4–6 Fr urinary catheter is used with a 12–14 G intravenous catheter, depending on patient size

Complications can include subcutaneous emphysema, pneumomediastinum, pneumothorax, bleeding, catheter breakage and aspiration of the catheter into the airway, and worsening respiratory status due to the stress of the procedure

Endotracheal wash

Endotracheal washes can be used in small dogs, large dogs that have been anaesthetized for another procedure and cats. The patient should be stable enough to be lightly anaesthetized

1. A sterile endotracheal tube is inserted into the trachea, avoiding oral contamination.
2. A sterile dog urinary catheter or red rubber catheter is used to inject sterile saline beyond the lumen of the endotracheal tube.
3. The catheter is then aspirated while an assistant performs coupage on the patient.

An alternative method uses a suction catheter and sterile suction trap to collect the sample. This requires mechanical suction; the sample is automatically collected into the sterile suction trap

Patients that have an endotracheal wash performed should be closely monitored during recovery to ensure that they have adequate ventilatory function and oxygenation

7.15 Tracheal washes.



7.16 Trans-tracheal wash. (a) The ventral neck of the dog is clipped and aseptically prepared. (b) An 18 G through-the-needle catheter is pushed through the skin and 'popped' into the trachea between two tracheal rings. (c) The catheter is angled downward and fed all the way into the trachea. The sterile sheath is removed, the needle is withdrawn and the needle guard replaced, and the stylet is removed. (d) Sterile saline is flushed into the catheter and the catheter is then aspirated to obtain the sample.

Syndromes of lower airway disease

Feline allergic bronchitis: Feline allergic bronchitis, also referred to as feline asthma, is the most common cause of lower airway disease in cats (Figure 7.17). The clinical signs result from bronchial inflammation with peribronchial infiltrates, mucosal oedema, increased mucus production, bronchiolar smooth muscle hypertrophy, and reversible airway obstruction caused by excessive bronchoconstriction due to smooth muscle spasm. Airway obstruction is most severe during expiration and may lead to air trapping and alveolar hyperinflation. Cats may present with disease at any age but signs often first appear in young adults.

- Feline asthma
- Chronic bronchitis
- Neoplasia
- Aspirated foreign body

7.17 Common differential diagnoses for lower airway disease in dogs and cats.

Clinical signs can range from severe dyspnoea to intermittent cough. In severe cases, cats exhibit open-mouth breathing, have pale to cyanotic mucous membranes and may have an abdominal component to respiration, especially during expiration. On auscultation, expiratory wheezes are often heard. In the most severe cases, respiratory sounds may be virtually absent, as air movement is almost cut off by the severity of bronchial obstruction.

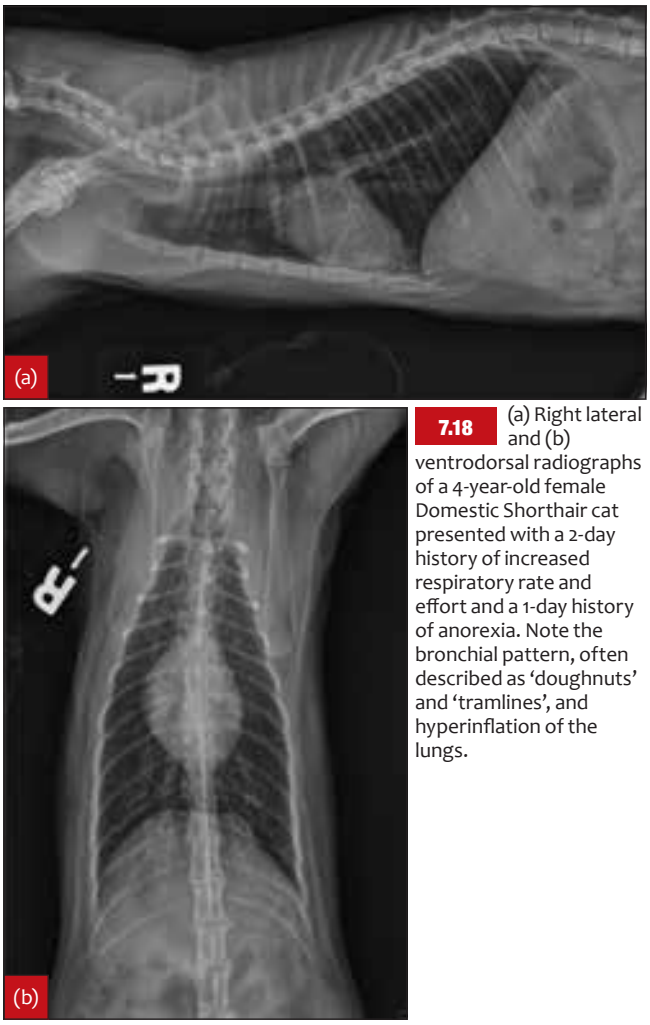
If the cat is in severe distress, obtaining a definitive diagnosis should be delayed until it is more stable. The cat should be placed in an oxygen cage, thereby minimizing stress and allowing it to relax after transport. Since bronchoconstriction occurs as a result of inflammation, corticosteroids should be given intravenously if possible (otherwise, intramuscularly). Bronchodilators such as terbutaline have proven to be useful in acute management. In agonal cases, adrenaline (epinephrine) should be administered (0.5–0.75 ml of 1:10,000 solution i.m.) for its profound vasoconstrictive, inotropic and bronchodilator effects. If there is no response to medical management and the cat remains in severe distress, anaesthesia (halothane is particularly useful for its bronchodilatory effects) and intubation may be required. Occasionally, cats may have pneumothorax secondary to rupture of the hyperinflated alveoli.

Radiographic findings include a bronchiolar pattern, collapse of the right middle lung lobe and pulmonary hyperinflation (Figure 7.18). Findings may be normal if radiography is delayed until the patient has been stabilized. Definitive diagnosis requires the demonstration of inflammation on tracheal wash cytology.

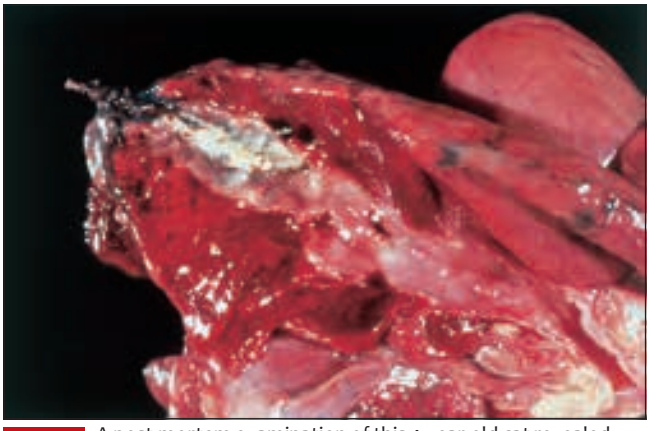
Canine chronic bronchitis: This is characterized by a persistent cough occurring for at least two consecutive months in the absence of another specific pulmonary disease. Hyperplasia and hypertrophy of the bronchial glands, increased goblet cells, increased airway secretions and increased infiltrates of inflammatory cells are seen. This results in thickened, hyperaemic bronchial walls, obstruction of small airways with mucus and proliferation of epithelial surfaces. Patients with exacerbated or end-stage disease can present with severe distress and cyanosis.

Physical examination findings may include increased airway sounds with wheezes and coarse crackles on chest auscultation caused by opening and closing of small bronchi. Thoracic radiographs usually show a bronchial pattern, and the extent of the changes does not always correlate with the severity of clinical signs. Severe cases may show evidence of bronchiectasis. Immediate management is as described above. In addition, saline nebulization may assist with mobilization of secretions.

Lower airway masses and foreign bodies: Foreign bodies and tumours can also occur in the lower airways. Radiographs may assist in confirming the diagnosis. Chronic bronchial obstruction causes gradual collapse and absorption atelectasis of the affected lung lobe. Even if a foreign body or neoplasm is not visible on radiographs, the presence of one completely collapsed lung lobe should prompt suspicion of complete bronchial obstruction and absorption atelectasis. Sudden onset of respiratory distress can be seen after aspiration of a foreign body into the bronchi (Figure 7.19). Foreign bodies may be retrieved with the aid of bronchoscopy or fluoroscopy or removed at the time of thoracotomy. Neoplasia of the lower airways is usually characterized by a slower, more gradual onset of respiratory distress. Thoracic radiographs and bronchoscopy can aid in diagnosis, and biopsy assists in its confirmation. Debulking or removal of the mass (often including lung lobectomy) may be necessary, unless the biopsy reveals lymphoma, which may respond to chemotherapy.



7.18 (a) Right lateral and (b) ventrodorsal radiographs of a 4-year-old female Domestic Shorthair cat presented with a 2-day history of increased respiratory rate and effort and a 1-day history of anorexia. Note the bronchial pattern, often described as 'doughnuts' and 'tramlines', and hyperinflation of the lungs.



7.19 A post-mortem examination of this 4-year-old cat revealed aspirated plant material in a bronchus.
(Reproduced with permission of Veterinary Learning Systems, Trenton, NJ)

Pulmonary parenchymal disease

Clinical signs

Clinical signs of pulmonary parenchymal disease are summarized in Figure 7.20. Pulmonary parenchymal disease is commonly associated with varying degrees of hypoxia and respiratory distress. The lungs typically have decreased compliance, resulting in a restrictive pattern of respiration (rapid shallow breathing), and severe hypoxia may be manifested by paradoxical respiration. Hypoxia in patients with pulmonary parenchymal disease is usually caused by ventilation/perfusion mismatch and even shunting due to filling and collapse of alveoli. Some patients may also have an increased diffusion barrier caused by thickening or infiltration of the alveolar membrane.

- Pale or cyanotic mucous membranes
- Increased respiratory rate or dyspnoea
- Restrictive respiratory pattern
- Harsh bronchovesicular sounds
- Crackles
- Nasal discharge
- Cough (often productive)

7.20 Clinical and historical signs associated with pulmonary parenchymal disease in dogs and cats.

On auscultation, harsh bronchovesicular sounds and/or crackles are common. Careful auscultation of the heart should be performed to detect the presence of a murmur, gallop or arrhythmia, which might indicate congestive heart failure. Nasal discharge can occur in patients with bronchopneumonia or profound pulmonary oedema. Coughing may be a feature of pulmonary parenchymal disease if there is bronchial irritation or inflammation. Typically, coughing is productive: a soft moist cough is an important part of clearance of secretions from the pulmonary parenchyma.

Animals with pulmonary parenchymal disease usually have an alveolar pattern on thoracic radiographs. The distribution of the alveolar pattern can provide important information about the aetiology of respiratory failure. Occasionally, animals may have minor or absent radiographic changes (e.g. with pulmonary thromboembolism or interstitial fibrosis).

General approach to management of patients with pulmonary parenchymal disease

The approach to management of animals with pulmonary parenchymal disease is summarized in Figure 7.21. Patients that are in respiratory distress due to suspected pulmonary parenchymal disease should receive oxygen supplementation immediately. Physical examination and historical findings often give an indication of the cause of the disease process. Thoracic radiographs are a valuable diagnostic tool. If respiratory distress is so severe that thoracic radiographs cannot be obtained safely, empirical treatment for the most common causes of pulmonary parenchymal disease should be initiated. For example, in cats presenting with severe dyspnoea and pulmonary crackles, which are most likely due to congestive heart failure, the intramuscular administration of furosemide may result in stabilization. Often, empirical medical management combined with oxygen supplementation can improve the condition of the patient to the point that radiographs can be obtained. If the patient does not improve or even deteriorates in spite of medical management, an aggressive approach may be required, including general anaesthesia and intubation of the patient to facilitate diagnostic testing and therapy.

- Oxygen supplementation
- Rest and minimal stress
- Vascular access
- Thoracic radiographs (if possible)
- Medical management according to most likely differential diagnoses:
  - Bacterial bronchopneumonia:
    - Tracheal wash for culture and cytological examination

    Stable:
    - Enrofloxacin at 5–15 mg/kg orally q24h *or*
    - Co-amoxiclav at 14–22 mg/kg orally q12h

    Unstable:
    - Enrofloxacin at 5–15 mg/kg i.v. q24h and ampicillin at 22 mg/kg i.v. q8h *or*
    - Amikacin at 15 mg/kg i.v. q24h and ampicillin at 22 mg/kg i.v. q8h *or*
    - Cefotaxime and clindamycin at 11 mg/kg i.v. q12h *or*
    - Ticarcillin/clavulanate at 50 mg/kg i.v. q6h (currently not available in the USA)
    - Nebulization and coupage
  - Pulmonary oedema:
    - Furosemide at 0.5–2 mg/kg i.v., i.m. q4–12h
    - Glyceryl trinitrate paste at 6–25 mm cutaneously *or*
    - Pimobendan at 0.15 mg/kg i.v. q12h
    - Nitroprusside at 2–10 µg/kg/min
    - Dobutamine at 5–10 µg/kg/min
  - Haemorrhage (due to coagulopathy):
    - Fresh whole blood or fresh frozen plasma transfusions
    - Vitamin K1 at 2 mg/kg s.c., orally q12h
  - Pulmonary thromboembolism:
    - Unfractionated heparin at 100–300 IU/kg s.c. q6h *or* 10–50 IU/kg/h i.v. constant rate infusion
  - Pulmonary inflammatory disorders:
    - Dexamethasone at 0.25–0.5 mg/kg i.v., i.m. q12–24h *or*
    - Prednisolone at 0.5–1 mg/kg i.v., i.m., orally q12–24h

7.21 General approach to emergency management of dogs and cats with pulmonary parenchymal disease.

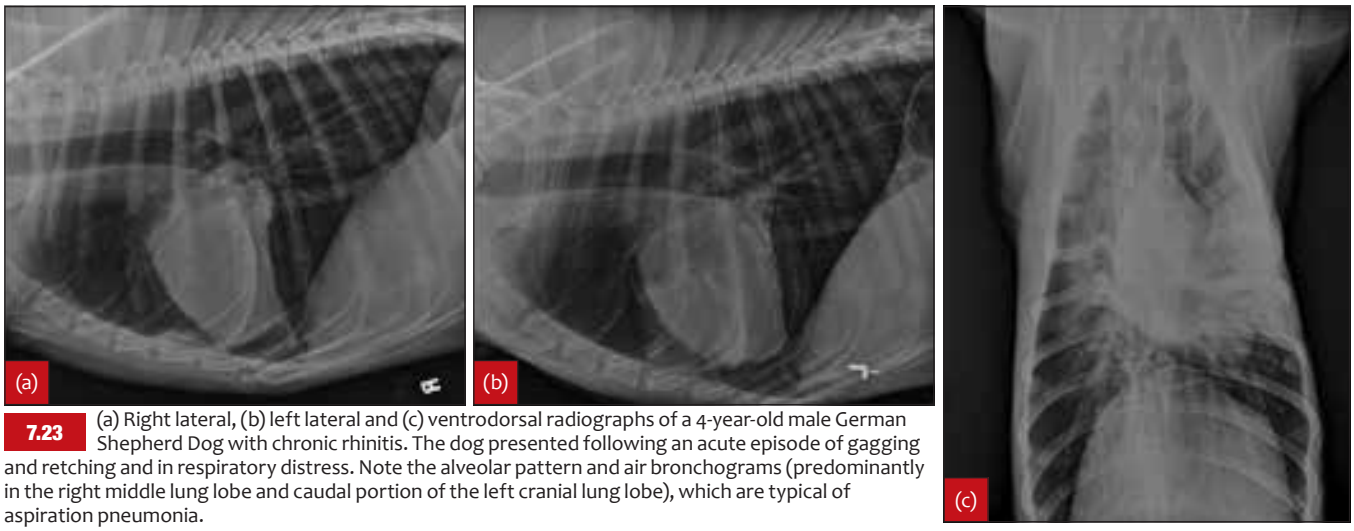
Syndromes of pulmonary parenchymal disease

Pneumonia: This is one of the most common causes of pulmonary parenchymal disease (Figure 7.22). Pneumonia is categorized as aspiration, bacterial, parasitic, viral or fungal, occurring alone or in combination. Pneumonia is more common in dogs than in cats. Physical examination usually reveals increased respiratory rate and effort, pale to cyanotic mucous membranes, and harsh lung sounds or crackles. If the animal is stable, the diagnosis is confirmed by radiographic findings of alveolar disease (Figure 7.23), cytology showing acute neutrophilic inflammation, and culture and sensitivity testing of airway aspirates obtained by tracheal wash or bronchoalveolar lavage. Serology may be used to assist diagnosis of viral, parasitic or fungal pneumonia.

Aspiration pneumonia is caused by the inhalation of foreign material. This typically comprises oral secretions or gastrointestinal tract contents subsequent to vomiting or regurgitation. Animals with underlying conditions such as pharyngeal/laryngeal dysfunction, megaoesophagus, cleft palate, abnormal mentation, recumbency or debilitation have an increased risk of aspiration. The acidic pH of gastric reflux material determines the extent of bronchoconstriction and injury to the airway epithelium and pulmonary parenchyma. Liquids reach the alveoli within

- Pneumonia
- Pulmonary oedema (cardiogenic and non-cardiogenic)
- Haemorrhage
- Pulmonary thromboembolism
- Neoplasia: primary or metastatic
- Pulmonary inflammatory disease (PIE and LG)
- Acute lung injury and acute respiratory distress syndrome

7.22 Differential diagnoses for pulmonary parenchymal disease in dogs and cats. LG = lymphomatoid granulomatosis; PIE = pulmonary infiltrate with eosinophils.



7.23 (a) Right lateral, (b) left lateral and (c) ventrodorsal radiographs of a 4-year-old male German Shepherd Dog with chronic rhinitis. The dog presented following an acute episode of gagging and retching and in respiratory distress. Note the alveolar pattern and air bronchograms (predominantly in the right middle lung lobe and caudal portion of the left cranial lung lobe), which are typical of aspiration pneumonia.

minutes, making attempts to perform suction of the airways futile in most cases. The resultant inflammation impairs lung defences and allows bacteria in the aspirated material to colonize the lungs. By the time most aspiration pneumonia cases are recognized, bacterial infection has occurred. These patients are therefore treated in the same way as those with primary bacterial pneumonia. In patients with severe dyspnoea immediately after an acute aspiration event, transient but profound bronchoconstriction may be the cause of acute hypoxia. Some of these patients respond very well to the intravenous administration of a bronchodilator such as terbutaline.

Bacterial bronchopneumonia usually occurs as a consequence of bronchogenous invasion (inhalation or aspiration) of pathogenic and opportunistic bacteria, or occasionally by haematogenous spread. Animals with bronchogenous pneumonia typically have a cranioventral pattern of alveolar disease on radiographs, whereas those with haematogenous pneumonia often have a patchy or nodular distribution. Bacterial pneumonia can be caused by primary respiratory tract pathogens, such as *B. bronchiseptica*, or by opportunistic pathogens that proliferate because of suppression of respiratory tract defences. With the exception of animals suspected of *Bordetella* spp. infection, dogs and cats that present with bacterial pneumonia should be carefully evaluated for underlying disorders.

Other causes of pneumonia include parasites (*A. vasorum*), viral agents (canine distemper and canine influenza), protozoal organisms (toxoplasmosis) and fungal invasion (histoplasmosis, blastomycosis and coccidioidomycosis). In addition to general pneumonia management, specific therapy should be directed against individual organisms.

Bacterial cultures should be obtained before starting antibiotic therapy whenever possible. Gram-negative pathogens and polymicrobial infections are common. Broad-spectrum antibiotic treatment should be started while waiting for the culture results. Oral drugs such as trimethoprim/sulphonamides, chloramphenicol, co-amoxiclav or fluoroquinolones can be used if the animal is not systemically ill. If the patient is hypoxic, in respiratory distress or febrile, intravenous antibiotics must be administered until the animal is stable. Combinations of antibiotics that provide broad-spectrum coverage include ampicillin/aminoglycosides, ampicillin/fluoroquinolones or a second- or third-generation cephalosporin combined with clindamycin. Another potentially valuable therapy is nebulization with sterile saline followed by coupage to loosen and mobilize airway secretions, promote coughing and improve airway clearance. Nebulized mucolytic agents are not typically used as they can cause bronchospasm, but mucolytic drugs such as acetylcysteine or guaifenesin can be used intravenously or orally. Oxygen supplementation should be administered as required, and severely affected cases may require positive pressure ventilation (PPV).

Pulmonary oedema: This is the accumulation of fluid in the alveoli and pulmonary interstitium and is divided by initiating cause into cardiogenic and non-cardiogenic forms. Cardiogenic oedema is more common and is seen in animals with left-sided heart failure and elevated pulmonary venous pressure. On auscultation, crackles are often evident and may be accompanied by a mitral murmur in dogs or a gallop rhythm in cats. Thoracic radiographs usually reveal cardiomegaly and a perihilar alveolar pattern in dogs. In cats, distribution of oedema is less specific. Details of diagnosis and management of cardiogenic pulmonary oedema are given in Chapter 6.

Neurogenic pulmonary oedema is a form of non-cardiogenic pulmonary oedema that can be caused by seizures or head trauma, choking or airway obstruction, and electric shock. Acute stimulation of specific areas of the brainstem triggers a massive, but transient, reflex sympathetic discharge that results in increased peripheral vascular resistance, briefly raising systemic blood pressure. Blood therefore moves transiently from the systemic circulation into the low-pressure pulmonary vasculature, which has relatively few catecholamine receptors. This volume shift dramatically and transiently elevates pulmonary venous pressures. The resultant increase in hydrostatic pressure (transmural pressures often >40 mmHg) causes capillary wall stress, which damages the capillary endothelial cells and the basement membrane, leading to an acute increase in microvascular permeability. The end result is fluid redistribution into the interstitium and alveoli. The pressures rapidly return to normal, but the changes in permeability remain for several hours.

Affected animals may develop respiratory distress immediately or over several hours after the inciting incident. Varying degrees of respiratory distress occur; some animals have minimal signs, whilst others can rapidly become agonal because of fulminant pulmonary oedema. Crackles are often heard on auscultation. The diagnosis can be confirmed by thoracic radiography, which reveals an interstitial or alveolar pattern typically in the dorsocaudal

lung fields (Figure 7.24). The extent of lung impairment is determined by arterial blood gas analysis. Animals are hypoxic and have a P_aCO_2 that may be low, normal or high, depending on the severity of the disease.

Treatment consists of supportive care with oxygen supplementation as needed. Diuretics may be administered but are less effective than in cardiogenic oedema because the oedema is caused by a vascular permeability change, rather than by a sustained increase in pulmonary venous pressure. The use of corticosteroids in these patients remains controversial and is not currently recommended. Mildly affected animals improve dramatically in 24–48 hours, while the most severely affected animals with fulminant pulmonary oedema may require PPV and often do not recover.



7.24 (a) Right lateral and (b) ventrodorsal radiographs of a 2-month-old male Cane Corso that presented with increased respiratory rate and effort after being choked when its lead became entangled with that of another dog. The dog was briefly unconscious after the incident. Note the bilateral alveolar pattern localized to both caudal lung lobes; this is the classic pattern and distribution seen with non-cardiogenic oedema.

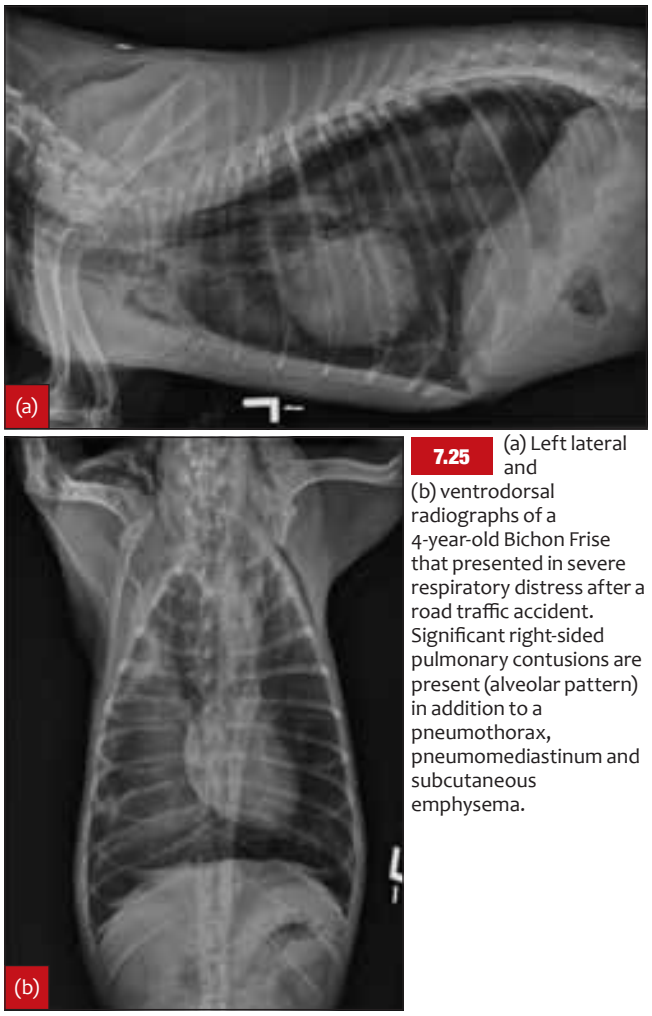
Lungworms: These parasitic nematodes can cause clinical signs of respiratory disease, including coughing and dyspnoea. *A. vasorum* (French heartworm) is a metastrongylid nematode; the adult worm lives in the pulmonary arterioles. It can cause both respiratory signs and a coagulopathy, and is found most commonly in young dogs in the south of England. *Oslerus osleri* is found in small nodules on the mucosa of the tracheal bifurcation and bronchi of dogs and usually causes coughing, but occasionally can cause dyspnoea due to airway obstruction. *Aelurostrongylus abstrusus*, which primarily infects cats, is found in the terminal bronchioles and alveoli and causes bronchiolitis and pneumonia. *Filaroides hirthi* and *Crenosoma vulpis*, which are found in the lower airways of dogs, cause bronchitis and eosinophilic or granulomatous pneumonia. Both dogs and cats can be infected with *Capillaria aerophila*, which lives in coiled masses embedded in the tracheal and bronchial mucosa and causes chronic coughing or pneumonia. Occasionally, dogs and cats heavily infested with ascarids may have respiratory signs associated with lung migration.

Radiographic signs are generally non-specific, although a peripheral alveolar–interstitial pattern has been reported with *Angiostrongylus vasorum* infection and mucosal nodules are occasionally visible with *Oslerus osleri*. As the life cycle of most parasites involves production of first-stage larvae in the lung, which are then expectorated into the mouth and swallowed, diagnosis is achieved by identifying larvae in faeces (Baermann technique or direct smear). Larvae may also be identified in tracheal wash samples, along with neutrophilic or eosinophilic inflammation. There is also an antigen blood test available in the UK that is specific for the detection of *A. vasorum* infection. *O. osleri* nodules and adult parasites may be directly visualized with bronchoscopy. Although some parasites (such as *O. osleri* and *F. hirthi*) are directly transmitted, most other lungworms require a paratenic host such as a slug, snail or earthworm. Treatment of lungworms typically involves the use of fenbendazole, milbemycin or moxidectin. Fenbendazole should be administered for a minimum of 14 days and as long as 20 days in cats with *A. abstrusus*.

Pulmonary haemorrhage: Pulmonary haemorrhage can occur secondary to trauma (pulmonary contusions), coagulopathies (anticoagulant rodenticide ingestion, *A. vasorum* infection) and neoplasia. Haemorrhage into the parenchyma is commonly seen following anticoagulant rodenticide ingestion. These animals can present with coughing (which may include a productive cough with blood-tinged sputum), lethargy or respiratory distress. Varying degrees of anaemia and pale mucous membranes are seen due to blood loss. Radiographs usually reveal a patchy alveolar pattern or pleural effusion. Treatment consists of oxygen support, fresh frozen plasma or fresh whole blood in addition to vitamin K1 therapy (see Chapters 14 and 19).

Pulmonary contusions are the second most common cause of respiratory distress following blunt thoracic trauma, representing haemorrhage into the pulmonary interstitium and alveoli from ruptured capillaries (Figure 7.25). These animals are often in hypovolaemic (haemorrhagic) shock, combined with respiratory distress and increased bronchovesicular sounds or even crackles. Even though these patients are usually in shock, caution should be exercised when giving intravenous fluids, since fluid loading can worsen the severity of pulmonary haemorrhage and can cause accumulation of oedema in addition to blood. Although crackles may sometimes be heard on chest auscultation, diuretics are contraindicated in the presence of shock. Diuretics do not prevent further haemorrhage into the pulmonary parenchyma nor promote reabsorption of erythrocytes from the lung. Rather, by causing diuresis, they may exacerbate hypovolaemia.

Pulmonary contusions should be treated with cautious fluid therapy and supportive care (oxygen supplementation) until the lungs have a chance to reabsorb the blood. In severe cases, PPV and/or positive end-expiratory pressure (PEEP) may be required to support oxygenation. If pulmonary function deteriorates following fluid therapy but



7.25 (a) Left lateral and (b) ventrodorsal radiographs of a 4-year-old Bichon Frise that presented in severe respiratory distress after a road traffic accident. Significant right-sided pulmonary contusions are present (alveolar pattern) in addition to a pneumothorax, pneumomediastinum and subcutaneous emphysema.

the cardiovascular system has stabilized, it is likely that pulmonary oedema is present superimposed on the haemorrhage. In this event, judicious use of furosemide can be helpful to resolve the oedema.

Bacterial pneumonia is an uncommon complication of pulmonary contusions, but prophylactic antibiotic therapy is not recommended. Prophylactic antibiotics result in selection for resistant bacterial populations and may not change the incidence of pneumonia. Instead, the patient should be monitored for signs that pneumonia has developed: a productive cough, fever or failure of respiratory signs to resolve within 48–72 hours. If pneumonia occurs, a tracheal wash with culture and sensitivity testing is recommended, followed by appropriate antibiotic therapy, nebulization and coupage.

Pulmonary thromboembolic disease: This is caused by pulmonary arterial obstruction by thrombi and results in respiratory distress by producing severe ventilation/perfusion mismatch. Thrombi form because of systemic hypercoagulability, stasis of blood within vessels or direct endothelial damage. Thrombi can form in disease states such as protein-losing nephropathy, hyperadrenocorticism, immune-mediated haemolytic anaemia, bacterial endocarditis, dirofilariasis, sepsis and pancreatitis, as well as following surgery (see Chapter 13). Affected patients often have a sudden onset of respiratory distress, increased respiratory rate and effort, generalized harsh lung sounds, and pale to cyanotic mucous membranes. When thrombus accumulation in the lungs is extensive, an occlusive reduction in pulmonary venous return to the heart may occur, which is detected as reduced pulse quality and hypotension. Thoracic radiographs are often normal but may reveal varying interstitial or alveolar patterns, pleural effusion and dilated or truncated pulmonary arteries (Figure 7.26). The most common clinicopathological findings are elevation of serum D-dimers and thrombocytopenia. A definitive diagnosis can sometimes be made using non-selective CT angiography, but unstable patients may not tolerate this procedure because of the need for anaesthesia. Newer techniques using very fast scanners are now allowing CT imaging in conscious patients, and the information obtained is often useful despite motion artefacts occurring during respiration. Even if CT is not diagnostic for a thrombus it can provide an alternative diagnosis.



7.26 Lateral thoracic radiograph of a mixed-breed dog with severe autoagglutinating haemolytic anaemia that developed acute respiratory distress. A presumptive diagnosis of pulmonary thromboembolism was made based on the severity of the hypoxia and lack of radiographic abnormalities.

The prognosis for thromboembolic disease is fair to guarded depending on the extent of lung involvement and the nature of any underlying disease condition. Oxygen supplementation should be provided but may not lead to dramatic improvement because of pulmonary shunting. Therapy consists of supportive care, treatment of the underlying disease and prevention of further thrombosis using anticoagulants. Heparin can be administered subcutaneously or as an intravenous constant rate infusion (see Figure 7.21) or clopidigrel can be given orally. If the predisposing disease is established and considered ongoing, warfarin therapy can also be instituted for long-term maintenance. In such cases, treatment with heparin is tapered and discontinued. Thrombolytic agents such as tissue plasminogen activator have been used with mixed success in a limited number of patients (see Chapter 13).

Neoplasia: Primary pulmonary neoplasia or metastatic disease can also cause severe respiratory distress. Patient history varies from acute signs to a gradual onset of exercise intolerance and laboured breathing with or without coughing. Thoracic radiographs and identification of a distant primary neoplasm are often diagnostic. A definitive diagnosis may be obtained following cytological examination of pleural fluid or FNA of the mass. If cytological evaluation and other diagnostic tests provide equivocal results, exploratory thoracotomy may be required. Supportive care should be provided as needed, but treatment

options may be limited. Unless the neoplasm is either responsive to chemotherapy or can be removed in its entirety (or at least debulked) at the time of surgery, euthanasia is often indicated.

Pulmonary inflammatory disease: This is an uncommon cause of respiratory distress in small animals. Reported pulmonary inflammatory diseases include pulmonary infiltrate with eosinophils and lymphomatoid granulomatosis. Pulmonary tissue is infiltrated by a non-neoplastic proliferation of eosinophils or lymphocytes, respectively. Clinical findings vary from sudden to gradual onset of respiratory distress or coughing. Radiographic findings include mass lesions or infiltration. The diagnosis may be confirmed by a cytological finding of inflammatory cells on samples obtained by tracheal wash or FNA. Other underlying causes such as pulmonary parasites must also be ruled out. Apart from routine respiratory supportive care, therapy includes immunosuppressive doses of corticosteroids. More aggressive cytotoxic drugs may be required in refractory cases. Many animals respond well to therapy.

Acute lung injury and acute respiratory distress syndrome: ALI and ARDS are terms that refer to a syndrome of generalized inflammatory lung injury. Inflammation can be triggered by systemic inflammatory disorders (such as septic shock or pancreatitis) or by a severe pulmonary insult (such as aspiration pneumonia, pulmonary contusions or smoke inhalation). In ALI, mild to moderate pulmonary inflammation manifests as vasculitis, interstitial and alveolar permeability oedema, and infiltration of inflammatory cells such as neutrophils and macrophages. ARDS is a more severe form, manifested by inflammation as in ALI, accompanied by proliferation of type II pneumocytes, hyaline membranes and eventually interstitial fibrosis. Animals with ALI-like syndrome have mild to moderate degrees of respiratory distress and hypoxia, and often respond to fluid restriction, low doses of diuretics and treatment of the underlying disease. Despite the fact that this is an inflammatory disease, corticosteroids have been shown to have no effect on mortality rates in humans with these syndromes, and may be contraindicated because of their immunosuppressive effects. Animals with ARDS have severe pulmonary dysfunction and very poor lung compliance. They usually require PPV and the prognosis is grave.

Pleural space disease and disruption of the thoracic cage

Clinical signs

The clinical signs of pleural space disease are summarized in Figure 7.27. Pulmonary dysfunction can be caused by the accumulation of fluid, air or soft tissue within the pleural cavity. Pleural space disease is suggested by physical examination findings that include increased respiratory rate or effort, dyspnoea and auscultation of diminished or dull lung and heart sounds. Depending on the cause, other signs such as fever may also be present. As the pleural pathology prevents lung expansion, hypoxia is caused by atelectasis and ventilation/perfusion mismatch. Radiographic changes are compatible with the presence of air, fluid or soft tissue density in the pleural space. Increased soft tissue density may occur secondary to neoplasia or diaphragmatic herniation into the pleural space.

- Increased respiratory rate and effort, short shallow respiratory pattern
- Dyspnoea
- Cough
- Dull or diminished lung and heart sounds on auscultation
- Fever
- Weight loss and lethargy

7.27 Clinical and historical signs associated with pleural space disease in dogs and cats.

General approach to management of patients with pleural space disease

The approach to management of patients with pleural space disease is summarized in Figure 7.28. If pneumothorax or pleural effusion is suspected and the animal is in severe respiratory distress, routine oxygen supplementation should be provided and thoracocentesis performed immediately, before imaging has confirmed the diagnosis. Thoracocentesis is both a therapeutic and a diagnostic procedure and can be life-saving in severely compromised patients (Figures 7.29 and 7.30). If a clinician feels uncomfortable performing thoracocentesis on the basis of physical examination alone, cage-side ultrasonography is recommended as the safest modality to confirm the presence of pleural fluid or air with minimal stress to the patient. Thoracic radiographs obtained after thoracocentesis are more valuable than those obtained prior to removal of the fluid or air. Once the fluid has been removed, radiographs may reveal the cause of the effusion, and allow evaluation of the cardiac silhouette and demonstration of masses.

Pleural effusions are classified according to the type of fluid obtained (Figure 7.31). Gross examination can identify whether the fluid is haemorrhagic, purulent, chylous or a transudate. All fluid should be analysed further, including determination of protein content, cytology and

- Oxygen supplementation
- Rest and minimal stress
- Vascular access
- Thoracocentesis
- Thoracic ultrasonography
- Thoracic radiography (if possible) after thoracocentesis
- Fluid analysis:
  - Cell counts
  - Cytology
  - Aerobic and anaerobic culture
  - Biochemical analysis if indicated (triglycerides)

7.28 General approach to emergency management of dogs and cats with pleural space disease.



7.29 Thoracocentesis is performed in this small dog using a butterfly catheter and a three-way stopcock.

Indications

- Patients with respiratory distress and dull lung sounds on auscultation
- Patients that present with dyspnoea after trauma (road traffic accident, bite wounds, falling from height)
- Patients that are undergoing positive pressure ventilation with sudden deterioration

Contraindications

- Severe coagulopathy

Procedure

Position the patient, preferably in sternal recumbency or standing. Lateral recumbency is also acceptable for pneumothorax. An assistant should be available to restrain the patient or give sedation as needed. In many cats a minimal restraint technique is preferred and is generally better tolerated.

1. Clip and aseptically prepare appropriate rib space:
   - If expecting fluid, the 7th or 8th intercostal space, at approximately the level of the costochondral junction
   - If expecting air, the 8th or 9th intercostal space, approximately one-third of the way down the chest.
2. Use sterile gloves for the insertion of the appropriate size needle or butterfly catheter:
   - Large dogs – 40 mm needle or even longer catheter
   - Medium sized dogs and large cats – 25 mm needle or catheter
   - Cats and small dogs – 18–22 mm butterfly needle.
3. Insert the needle slowly just cranial to the rib to avoid the intercostal blood vessels.
4. Observe the hub of the needle for any signs of fluid:
   - If a small amount of frank blood is aspirated or if the lungs can be felt rubbing against the needle, the needle should be withdrawn and moved to a different location
   - If a large amount of blood is obtained, place 1–2 ml in an empty blood collection tube to see if it clots. Blood from haemothorax should not clot, while blood from the heart or a blood vessel should clot normally, if the patient does not have a significant coagulopathy
   - For any other fluid, aspiration should continue until no more can be removed.
5. Directing the needle ventrally, rolling the patient slightly to the side on which thoracocentesis is being performed, and re-aspirating from a more ventral location can facilitate removal of as much fluid as possible.
6. Fluid is retained for fluid analysis, cytology and possibly culture.
7. Aspiration of air will turn the tubing a slightly foggy, white colour as the warm air from the thoracic cavity encounters the room-temperature tubing.
8. Aspirate until negative pressure is reached. If negative pressure is never obtained, a tension pneumothorax may be present, and chest tubes with continuous suction are needed (see Figure 7.32).

7.30 Thoracocentesis

- Pleural effusion:
  - Pyothorax
  - Non-bacterial exudates (FIP or neoplasia)
  - Chylothorax
  - Transudates (pure or modified)
  - Haemothorax
  - Sanguineous effusions (lung lobe torsion)
- Pneumothorax
- Diaphragmatic hernia
- Pleural neoplasia or masses

7.31 Common differential diagnoses for pleural space disease in dogs and cats. FIP = feline infectious peritonitis.

cell counts. In addition, specific chemical analysis such as triglyceride concentration or microbiological culture may be indicated. The character of the pleural effusion determines the course of further diagnostic evaluation and the likelihood of recurrence. Specific management depends on the results of fluid analysis and presence of underlying disease.

Syndromes of pleural space disease

Pyothorax: This is the accumulation of a purulent exudate in one or both sides of the pleural space and is more common in cats than in dogs. The aetiology includes idiopathic causes, penetrating chest wounds, haematogenous spread, extension from adjacent structures or fascial planes, aspirated foreign bodies, ruptured pulmonary abscesses and ruptured oesophagus. Presenting complaints include lethargy, anorexia, respiratory distress, fever and/or weight loss. The diagnosis is confirmed by high nucleated cell counts in the pleural fluid with a large number of degenerate neutrophils. Bacteria may be visible but are not always evident. Both aerobic and anaerobic cultures should be submitted because of the high incidence of anaerobic bacteria in pleural infections. Polymicrobial infections are common.

Treatment in cats should consist of thoracic drainage and administration of broad-spectrum intravenous antibiotics until the rate of effusion diminishes, followed by oral antibiotics once culture results become available. Since this is a deep tissue infection, prone to recurrence in individual animals, antibiotic therapy is typically continued for 2–3 months. Thoracic drainage can be accomplished by repeated needle thoracocentesis; however, it is a painful procedure that may not be well tolerated, and may not effectively drain the exudate if it is viscous or loculated. Placement of one or more chest drains allows continuous drainage of the fluid as it forms (Figures 7.32 and 7.33). Frequency of drainage depends on the rate of fluid production, but gentle aspiration of the chest tube is usually performed several times daily. Alternatively, the drain may be attached to a pleural suction device, which provides gentle continuous negative pressure to the drain and is ideal if large volumes of fluid are produced. Lavage of the thoracic cavity with 5–20 ml/kg of warmed sterile saline once or twice daily has been recommended but should be reserved for patients that have very viscous effusions; aseptic technique must be strictly followed to prevent a secondary infection. Thoracic drainage should continue until the fluid character has changed to a serosanguineous effusion containing non-degenerate neutrophils, and the volume has diminished to 5 ml/kg/day or less. On average, thoracic drainage is required for about 1 week but the range is from 2 days to 3 weeks. If patients fail to respond, careful evaluation for underlying causes of pyothorax, such as lung abscesses, should be considered and exploratory thoracotomy may be required.

In dogs, surgical treatment with thoracotomy has been shown to be beneficial in pyothorax, improving outcome and reducing recurrence rate when compared with medical therapy alone. The use of thoracoscopy for treatment of pyothorax in both dogs and cats has been discussed (Pelaez and Jolliffe, 2012). This treatment modality allows thorough lavage of the pleural space while guaranteeing removal of the fluid. It also provides an opportunity to examine the lungs and mediastinum for obvious abscessation, masses or foreign material. Thoracoscopy is frequently used in human patients with pyothorax, and has the potential to become the treatment of choice in veterinary patients as well.

Non-bacterial exudates: Feline infectious peritonitis virus can cause pleural effusion in affected cats, recognized by a sticky yellow effusion that has a high protein and low cellularity. The prognosis is very poor.

Indications

- Pyothorax
- Rapidly forming pleural effusion
- Recurring pneumothorax requiring repeated thoracocentesis
- Tension pneumothorax
- Postoperative management of thoracotomy patients

Contraindications

- Severe coagulopathy

Procedure

1. General anaesthesia (preferable); can be done with sedation only in an emergency.
2. Place the patient in lateral recumbency.
3. Clip the lateral thorax from just caudal to the front legs to the last rib and from the dorsal spine to the ventral midline.
4. Aseptically prepare and drape the area.
5. Loosen stylet from the chest tube. Extra holes can be carefully made in the chest tube to aid drainage if fluid is present in the pleural space. The holes are made with a scalpel blade and should not exceed 50% of the diameter of the tube to prevent tube breakage within the thoracic cavity.
6. A small stab incision should be made in the skin over the highest point of the thorax at intercostal space 9–10.
7. The skin is then pulled forward (by the assistant) to create a tunnel and allow the chest tube to be placed in intercostal space 7–8 (Figure 7.33a).
8. Lidocaine (maximum total dose of 7 mg/kg) is injected into the intercostal muscles at the point of tube insertion or an intercostal block can be performed, injecting lidocaine just ventral and caudal to transverse processes of the thoracic vertebrae/head of ribs one space cranial and caudal, and at the site of insertion. Before injecting, aspirate to determine that the needle is not in the intercostal artery or vein.
9. Haemostats are used to dissect bluntly into the pleural space, then spread wide enough to allow the tube to be passed through the hole created. The tube and stylet are inserted into the pleural space and advanced very slightly as a unit in a cranioventral direction. At this time, the tube/stylet should be being held parallel to the thoracic wall. The tube should then be fed off the stylet in a cranioventral direction. Tubes without trochars can also be placed using this technique.
10. Stop manual ventilation while inserting the tube, to allow the lungs to deflate and decrease the risk of trauma to the lungs.
11. Assess placement of the tube by using the stylet to measure the distance the tube has been advanced within the thorax.
12. Connect the tube to a three-way stopcock and injection caps or a pleural drainage system.
13. As soon as the drain is in place, aspirate as much of the air/fluid as possible. Record the amount and keep samples for further analysis if required.
14. Secure to the skin with a purse-string suture around the tube at the entry site and a 'Chinese finger trap' suture pattern to reduce sliding of the tube.
15. Place a sterile dressing and light bandage.
16. Tube connection sites can be secured with orthopaedic wire in figure-of-eight patterns.

Alternative method – trochar technique

1. Sedation or anaesthesia should be provided, if possible.
2. Steps 2–6 as above.
3. The tube is tunnelled subcutaneously two to three rib spaces (Figure 7.33b), then positioned perpendicular to the chest wall and grasped tightly 2.5–5.0 cm from its distal tip to prevent the tube from penetrating too deeply into the chest cavity.
4. The top of the tube is hit bluntly with the palm of the other hand, popping the tube through into the pleural space.
5. The tube is then slid off the stylet, directed cranially and ventrally, then connected and secured as above.

This is a very rapid placement technique, but is not recommended unless in an emergency situation with no other options, due to increased risk of iatrogenic trauma. It is never recommended in cats due to their small size and very compliant chest walls.

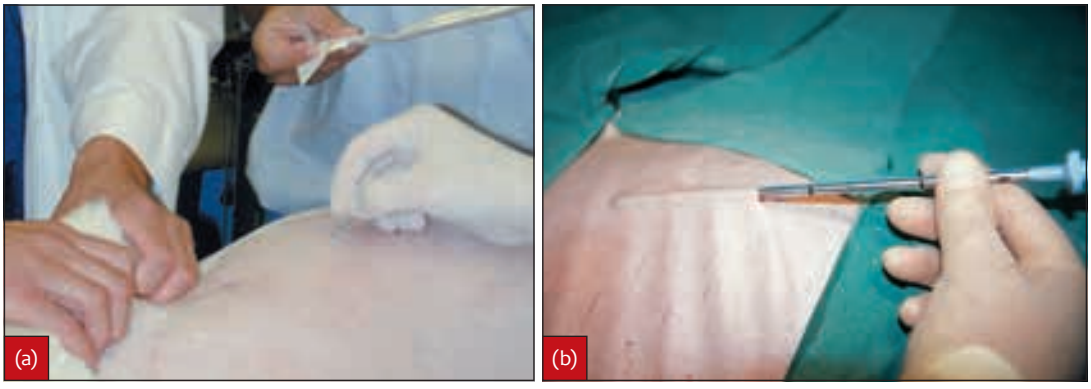
Alternative method – Seldinger technique

1. An over-the-wire technique similar to that used to place central venous catheters may be used. Kits are available.
2. General anaesthesia is not usually required; the patient is usually lightly sedated.
3. A catheter is placed through the skin at rib space 9–10, tunnelled forward and then used to penetrate the thoracic wall at rib space 8 or 9.
4. A wire is placed through the catheter and the catheter removed.
5. The chest tube is threaded over the wire and the wire then removed.
6. The chest tube is then connected and secured as above.

Following placement (any method)

- Thoracic radiographs (lateral and ventrodorsal or dorsoventral) to check tube(s) placement should be performed
- The tube(s) should be securely bandaged to prevent patient interference. An Elizabethan collar may also be used
- Pain management with injectable opioids or intrapleural bupivicaine should be used. Non-steroidal anti-inflammatory drugs (NSAIDs) may be administered if the patient has a stable cardiovascular system
- Bupivicaine can be given at a dose of 1.5 mg/kg through the tube every 6–8 hours
- 24-hour monitoring is required due to the risk of disconnection and the development of pneumothorax

7.32 Chest tube placement.



7.33 Chest tube placement. (a) Prior to placement of the chest tube, the thoracic skin is pulled cranially by an assistant; release of the skin will create a subcutaneous tunnel for the tube. (b) The trochar thoracostomy tube has been inserted through a skin incision (10th intercostal space) and is being directed subcutaneously in a cranial direction. (a, courtesy of Dr D Holt; b, courtesy of Dr R White)

Chylothorax: This is the accumulation of a milky effusion within the pleural space, which has a triglyceride concentration higher than that of a concurrently obtained plasma sample. A true chylous effusion contains chylomicrons, but a pseudochylous effusion, although the same on gross inspection, contains only cholesterol. Chylothorax can occur whenever there is obstruction or leakage of chyle due to disruption of the thoracic duct (Figure 7.34). Common causes include idiopathic disease, trauma, neoplasia and feline cardiomyopathy.

Treatment of chylous effusion aims to remove the underlying cause and decrease the rate of formation. With the exception of chylous effusions caused by heart failure or lymphoma, where specific medical therapy is indicated, empirical medical management with Rutin (a flavonoid compound) and low-fat diets is often disappointing. Surgical management is associated with a poor prognosis for complete correction. Thoracic duct ligation accompanied by pericardectomy and omentalization of the thoracic cavity is generally regarded to be the best option, but is associated with a relatively high rate of recurrence. Recently, cisterna chyli ablation in addition to thoracic duct ligation has been recommended, and the combination of both of these procedures with pericardectomy may result in a better outcome. An alternative option is placement of a pleuro-peritoneal shunt device. Finally, subcutaneously placed pleuroports that allow repeated drainage of the pleural space by owners at home using a percutaneously placed Huber needle may allow mid- to long-term management of patients that have failed both medical and surgical management.



7.34 Lateral thoracic radiograph of a 5-year-old Domestic Longhair cat presented for progressive respiratory distress. The radiograph reveals a marked pleural effusion. Thoracocentesis was performed and 150 ml of a chylous effusion was removed.

Transudates: Pure and modified transudates are recognized as clear to yellow fluid, which has low cellularity and low protein content. The most common cause is right-sided congestive heart failure, management of which is discussed in Chapter 6. A complete cardiac evaluation should be performed and cardiac disease should be treated appropriately to prevent or reduce recurrence of pleural effusion. Transudates can also develop or be exacerbated by factors such as hypoproteinaemia and low oncotic pressure, or vasculitis. For these reasons, modified transudates in the pleural cavity are common in patients with sepsis or pancreatitis and in patients with pulmonary thromboembolism. Neoplasia may also cause a modified transudate, which may contain exfoliated neoplastic cells. This emphasizes the need for cytological evaluation of all effusions. Thoracic radiographs should be obtained following thoracocentesis to evaluate the cardiac silhouette and to look for evidence of neoplasia. Occasionally, in the absence of cardiac disease, a definitive diagnosis cannot initially be made. As the disease progresses and the effusion returns, the underlying cause can usually be identified.

Haemothorax and sanguineous effusions: Haemothorax may be produced following trauma, as a result of a coagulopathy, or may be caused by neoplasia. Large, volume haemothorax is an uncommon complication of thoracic trauma. Dull ventral lung sounds, as well as decreased heart sounds, may be evident. Patients with significant haemothorax have usually sustained massive trauma to the chest cavity and other problems, including fractured ribs and pulmonary contusions, should be suspected. If the volume of pleural haemorrhage is small and respiratory distress is believed to be due to other causes (e.g. pulmonary contusions), then the pleural blood should not be removed. Minimal invasion of the chest prevents disruption of any clots that have formed and also allows resorption of erythrocytes and gradual 'autotransfusion'. If the animal has significant respiratory compromise because of blood in the pleural space, then thoracocentesis should be performed. In the most severe cases, an emergency thoracotomy may be required to identify and ligate a bleeding vessel.

Anticoagulant rodenticides are considered the most common non-traumatic cause of haemothorax. Animals with anticoagulant rodenticide poisoning may present in acute respiratory distress with no other obvious signs of bleeding. Treatment includes providing a source of coagulation factors via fresh whole blood or plasma transfusions, as well as vitamin K1 therapy. Thoracocentesis should only be performed if the animal's respiratory status is severely compromised by the pleural effusion, and preferably after the patient has been transfused with active clotting factors. Congenital coagulopathies such as haemophilia A can also lead to haemothorax but are less common. Neoplasms such as haemangiosarcoma can result in a rapidly forming haemothorax, which should be managed by transfusions and thoracocentesis (with cytological evaluation of the fluid). Patients that do not respond to conservative therapy may require exploratory thoracotomy to establish a diagnosis and to resect bleeding masses, although long-term prognosis is poor.

A sanguineous effusion can be defined as an accumulation of grossly bloody pleural fluid that does not have a high enough packed cell volume to be classified as haemorrhage. The most common causes of sanguineous effusions are lung lobe torsion and neoplasia. Lung lobe torsion is most commonly diagnosed in deep-chested dogs, with a predilection seen in Afghan Hounds and Borzois, although it has also been reported in Pugs. Affected animals present with an acute or chronic history of progressive dyspnoea and weight loss. On physical examination, typical findings include dull lung sounds in the ventral portion of the lung fields. Pleural fluid accumulates because of obstruction of venous outflow from the twisted lung lobe, and the fluid is typically bloody with numerous neutrophils and macrophages on cytology. Chylous effusions are also seen. Thoracic radiographs should be obtained after the fluid has been removed from the pleural cavity. The most common finding is complete collapse of a single lung lobe, which can appear consolidated or with an unusual 'honeycomb' pattern because of air trapped within the alveoli (Figure 7.35). The bronchus of the affected lobe may appear distorted or extend in the wrong direction. Ultrasonography with colour-flow Doppler

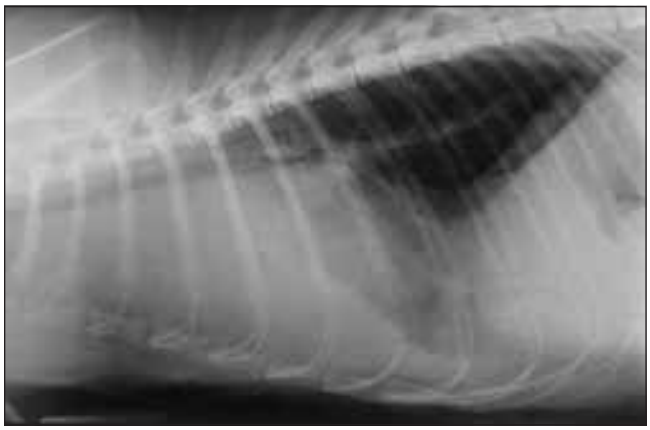




7.35 (a) Left lateral and (b) ventrodorsal radiographs of a 2-year-old female neutered Tibetan Terrier that presented with a 2-day history of lethargy, anorexia and vomiting several times. There is bilateral pleural effusion (worse on the right) and an alveolar pattern in the right middle lung lobe with a subtle vesicular appearance to the parenchyma. The main lobar artery appears narrowed on the lateral view and there are smaller air bronchograms in the lobe that are not oriented in the proper direction. There is also an alveolar pattern in the left cranial lung lobe. The dog was diagnosed with a lung lobe torsion and taken to surgery for a right middle lung lobectomy.

can help confirm the diagnosis by showing lack of blood flow in the affected lung lobe. Once lung lobe torsion is suspected, an emergency thoracotomy is indicated to resect the affected lobe before tissue necrosis triggers the systemic inflammatory response syndrome (SIRS). If the lobe is resected early in the course of the disease process the prognosis is good, but occasionally effusions recur in the days and weeks following surgery. In these cases, the character of the effusion may change from sanguineous to chylous. The risk of chylous effusion appears to be particularly high in Afghan Hounds and Borzois, and in these breeds the prognosis for long-term survival is guarded.

Neoplastic effusions may also be sanguineous. Exfoliated neoplastic cells may be evident on cytological evaluation of the fluid, but the absence of neoplastic cells does not rule out neoplasia. The most common neoplasm that is easily diagnosed on cytology is lymphoma in cats, which is usually associated with a mediastinal mass that can reduce chest compressibility (Figure 7.36). Other neoplasms that can cause pleural effusion include carcinomas, chemodectomas, thymomas, sarcomas and mesotheliomas.



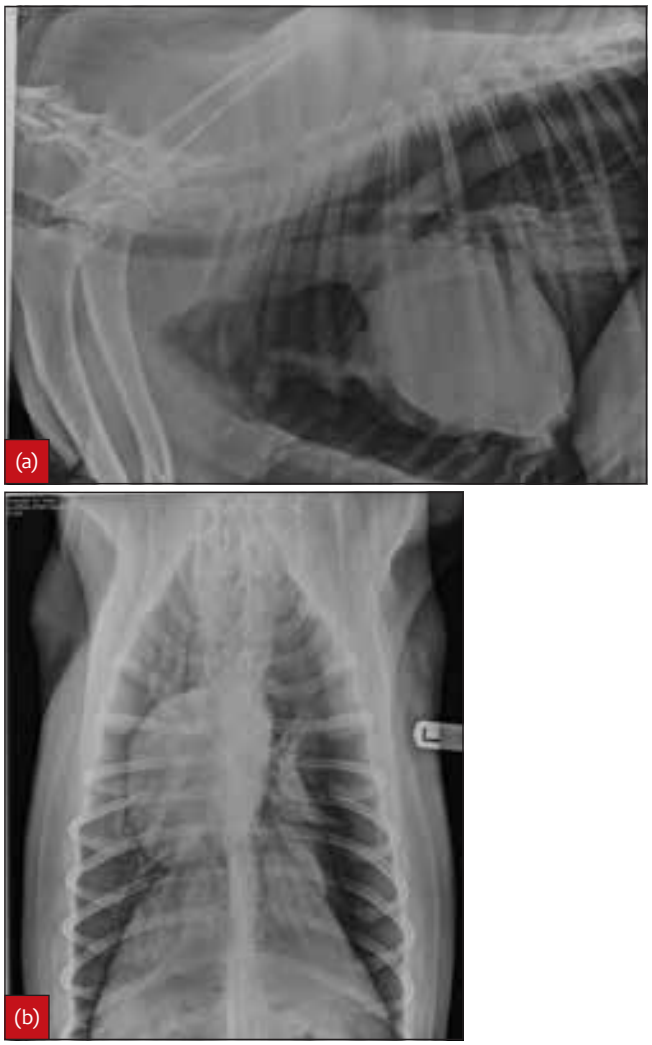
7.36 Lateral thoracic radiograph of a 9-year-old Siamese cat presented for increased respiratory rate and effort. Decreased chest compressibility and dull ventral lung sounds were noted on physical examination. The radiograph reveals a marked pleural effusion, elevation of the carina and narrowing of the trachea caused by a large mediastinal mass.

Pneumothorax: This can be defined as spontaneous or traumatic, and may be further classified as open, closed or tension. Blunt thoracic trauma commonly results in pneumothorax. It is caused by leakage of air from the parenchyma or airways into the pleural space, resulting in atelectasis or collapse of the lung lobes (Figure 7.37). Most cases of traumatic pneumothorax involve a small leak from the lung parenchyma, while injury to the trachea or mainstem bronchi is expected to cause pneumomediastinum with or without concurrent pneumothorax. Many trauma patients have a small air leak that quickly seals and may not lead to clinical signs. Where clinical signs of respiratory distress are absent and pneumothorax is an incidental finding on a screening radiograph, it is not necessary to remove the air as it will gradually be absorbed.

At the other end of the spectrum, tension pneumothorax is a serious condition in which a large pulmonary leak acts as a ball-valve, allowing air to enter the pleural cavity with each inspiration, but preventing air from leaving during expiration. This results in progressively increasing interpleural pressure, leading to further compression of the lungs and a mediastinal shift away from the pneumothorax. Tension pneumothorax is also associated with cardiovascular (obstructive) shock, as high interpleural pressures collapse the large veins and prevent venous return to the heart.

Open pneumothorax, typically as a result of a penetrating injury, is a life-threatening condition that can rapidly result in respiratory failure due to loss of negative pressure within the thoracic cavity and therefore loss of the ability to ventilate. This condition needs to be immediately recognized and treated appropriately. The wounds should be covered with a bandage to seal the thoracic cavity and the chest evacuated via either a chest tube or thoracocentesis; thoracic surgery is required to repair the chest wall defect once the patient has been stabilized. Alternatively, the patient can be anesthetized, intubated and ventilated with PPV until the thoracic wall is repaired.

Spontaneous pneumothorax can result from bullous emphysema, pulmonary blebs, neoplasia, asthma (in cats), fungal disease, heartworm, pneumonia, pulmonary abscesses, migrating foreign bodies, parasites and any other condition that might injure the lung parenchyma. In traumatic pneumothorax, the tear occurs in healthy lung tissue, whereas in spontaneous pneumothorax the leak occurs because of lung disease. Thus, in spontaneous pneumothorax cases, although the leak may temporarily



7.37 (a) Right lateral and (b) ventrodorsal radiographs of an 8-year-old male neutered Golden Retriever presented in acute respiratory distress. On auscultation there were very dull lung sounds, especially on the left side of the thorax. A spontaneous pneumothorax was diagnosed and at surgery a leaking bulla was found in the left cranial lung lobe. A partial lung lobectomy was performed.

seal following thoracocentesis, pneumothorax often recurs and the leak usually does not permanently seal on its own. Therefore, surgical exploration is recommended, with removal of any leaking or abnormal areas of lung to prevent recurrence of pneumothorax.

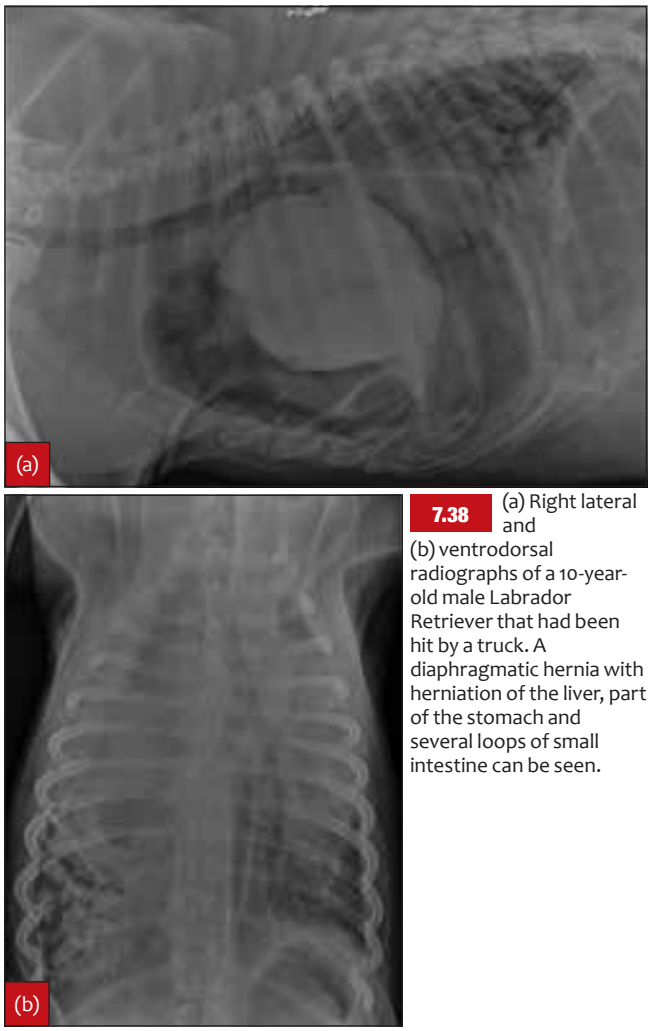
Animals with pneumothorax present with varying degrees of respiratory distress depending on the volume of air that is present in the pleural cavity. Physical examination findings include a rapid shallow respiratory rate, orthopnoea, pale, pink or cyanotic mucous membranes and diminished dorsal lung sounds. Concurrent signs of hypovolaemic shock (tachycardia, poor pulse quality or bounding pulses, and delayed or rapid capillary refill times) are common. These may be caused by concurrent haemorrhage in trauma patients or by obstruction of venous return to the heart due to the increased interpleural pressure exerted by a tension pneumothorax.

As pneumothorax is a common finding following road traffic accidents, the first priority for stabilization of any trauma patient in respiratory distress with dull lung sounds is to perform thoracocentesis even before radiographs are obtained. Similarly, if a spontaneous pneumothorax is suspected based on physical examination findings and history, thoracocentesis should be performed immediately. Most traumatic pneumothorax patients require thoracocentesis once or twice at presentation and, because the leak seals spontaneously, do not require further treatment for this problem. Some animals have a significant leak of air that continues after the initial thoracocentesis and, although they may show a good initial clinical response, they can develop respiratory distress again within minutes or hours of the procedure, necessitating repeated thoracocenteses. If needle thoracocentesis is required on more than three occasions, if the volumes obtained each time are large, or if the clinician fails to reach a negative pressure endpoint of thoracocentesis (probable tension pneumothorax), placement of a chest tube is indicated. If considerable volumes of air are leaking into the pleural cavity, management may be facilitated by attaching the chest tube to a water-sealed continuous evacuation device. These devices apply a negative pressure of 10–15 cmH_2O to the pleural cavity, simulating normal interpleural pressure, and continuously aspirate air from the chest as it leaks from the lungs. In most cases, the leak seals within 48 hours and no further treatment is necessary. On rare occasions, if the leak fails to seal, exploratory thoracotomy may be required to resolve the problem. Ongoing leaks that have failed to seal spontaneously may represent tears of major airways and are often accompanied by pneumomediastinum or subcutaneous emphysema.

Diaphragmatic hernia: Animals that have sustained trauma may also develop a diaphragmatic hernia (i.e. rupture of the diaphragm with penetration of abdominal contents into the thoracic cavity). A variety of organs may be involved in the hernia, including the liver, spleen, stomach, omentum and intestines (Figure 7.38). The physical presence of these organs, as well as the accumulation of pleural fluid due to inflammation and occlusion of venous return from the viscera, cause respiratory distress. Vascular compromise associated with strangulation may cause tissue necrosis, further compromising organ and pulmonary function. Acute onset of respiratory distress may occur if the stomach herniates and becomes bloated with gas due to occlusion of the cardia. The size of the stomach can increase rapidly due to gas distension. This represents an immediate surgical emergency and the gas distension of the stomach should be relieved by trocharization while the animal is being prepared for surgery.

Diagnosis of diaphragmatic hernia is suggested by clinical findings, including diminished lung sounds or auscultation of bowel sounds in the thorax. Some patients may also have signs of dysfunction relating to the displaced organs, such as vomiting or icterus. The diagnosis should be confirmed by (plain or contrast) radiography. If the stomach or intestines are located within the chest, they can be easily outlined by a small amount of oral barium. Other techniques, including positional lateral beam radiography, administration of intraperitoneal contrast media (e.g. iohexol) (Note: barium should *not* be used in the peritoneal cavity) or ultrasonography, can also provide valuable information.

Diaphragmatic hernias should be repaired surgically as soon as possible. Some patients with diaphragmatic hernia do not have clinical evidence of respiratory distress at the time of trauma and may present years later with the first signs of respiratory compromise. Animals with chronic diaphragmatic hernias may be extremely difficult to treat surgically because of the presence of adhesions and the high likelihood of postoperative re-expansion pulmonary oedema. Thus, early diagnosis and surgical treatment is



7.38 (a) Right lateral and (b) ventrodorsal radiographs of a 10-year-old male Labrador Retriever that had been hit by a truck. A diaphragmatic hernia with herniation of the liver, part of the stomach and several loops of small intestine can be seen.

essential for animals with this problem, even if clinical signs are not initially evident. Thoracic radiography is therefore recommended in all cases of trauma to rule out the presence of an occult diaphragmatic hernia.

Rib fractures and flail chest: Rib fractures are another common sequel of blunt thoracic trauma and are commonly accompanied by pulmonary contusions. Fracture of one or several ribs (Figure 7.39) does not usually require any specific treatment other than rest, pain management and oxygen supplementation. If several ribs are each fractured in more than one place, a flail chest segment can occur. The flail segment is not stabilized by attachment to the spine or sternum and can be observed moving paradoxically relative to the rest of the chest wall during respiration. During inspiration, when the rest of the chest is moving outward, the flail segment is pulled inward by negative intrapleural pressure.

Small to moderate-sized sections of flail chest should be managed medically, with oxygen supplementation and analgesia as needed. Respiratory distress in these patients is thought to be primarily caused by concurrent pulmonary contusions. Large flail chest segments can contribute to distress by preventing effective movement of the chest wall, resulting in hypoventilation. Placing the animal with the affected side down can help stabilize the segment and promote better ventilation. Large flail segments may require surgical stabilization, and some of these animals require postoperative mechanical ventilation if severe pulmonary contusions are also present.



7.39 Ventrodorsal radiograph of a 2-month-old male Pit Bull Terrier puppy after a road traffic accident. Fractures of ribs 4–9 can be seen on the left-hand side of the chest, in addition to severe pulmonary contusions.

Pulmonary function testing in the dyspnoeic patient

Apart from clinical examination, useful methods for pulmonary function testing in the dyspnoeic patient include arterial blood gas analysis, pulse oximetry and end-tidal capnography.

Arterial blood gas analysis

The most definitive method of assessing lung function is measurement of the partial pressure of oxygen (PO_2) and carbon dioxide (PCO_2) in arterial blood. Commonly used analysers directly measure pH, PO_2 and PCO_2. A variety of instruments is available to measure blood gases in veterinary practice, including relatively inexpensive hand-held instruments.

Samples of arterial blood can be obtained by direct puncture of any artery. Most commonly, the dorsal pedal (metatarsal) artery is used, but other sites include the femoral, brachial and auricular arteries. Samples can also be obtained from catheters placed in the dorsal pedal, femoral or auricular arteries (see Chapter 2). Blood gas syringes should be preheparinized, either by using heparin sodium solution to flush the syringe, or by use of specially made blood gas syringes which contain lyophilized lithium heparin.

To obtain a blood sample by direct puncture, one or two assistants are required to restrain the animal. The artery is palpated such that the operator can feel the pulsations with one hand and use the other to direct the needle at about a 60-degree angle towards the palpated artery. When the artery is penetrated, a flash of blood will be seen in the hub of the needle, and the syringe should

be aspirated to obtain the sample. Proprietary preset syringes contain a filter through which air is displaced and the syringe fills by direct arterial pressure, without the need for aspiration. On removal of the needle, direct pressure should be applied to the artery for a few minutes to prevent haematoma formation. All air bubbles should be removed immediately and the sample capped with an airtight seal to prevent exposure to room air. The sample should be analysed as soon as possible and kept on ice until analysis. Ideally, analysis should occur within 2 hours of sample collection.

A considerable degree of error can be introduced into blood gas analysis by operator technique and sample maintenance. If exposed to room air or if there are air bubbles in the sample, PCO_2 will decrease and PO_2 will increase as the sample equilibrates with room air gas tensions. Dilution of the sample with heparin also introduces error. Excessive heparinization of the syringe leads to a reduction in measured PCO_2, but little change in pH. This error can be minimized by expelling all of the heparin from the syringe after flushing, leaving only the heparin that fills the dead space in the hub of the needle, or by using lyophilized heparin.

Storage of the sample leads to changes in measured gas tensions as a result of ongoing metabolism by the cells. Anaerobic glycolysis by red blood cells leads to production of carbon dioxide. Oxygen utilization for aerobic metabolism by leucocytes and reticulocytes leads to a decrease in PO_2. The longer the sample is stored, and the higher the white cell count, the more pronounced these changes become. Maintenance of the sample on ice between collection and analysis minimizes this effect by reducing metabolism by the cells. Small samples of blood quickly cool to 0°C when placed in ice water and therefore do not maintain cell metabolism for more than a few minutes.

P_aO_2 and hypoxaemia

PO_2 represents the oxygen dissolved in plasma. The arterial partial pressure of oxygen (P_aO_2) determines the oxygen saturation of haemoglobin in a sigmoid relationship according to the oxygen dissociation curve (see Figure 7.2). **Haemoglobin is expected to be fully saturated at a P_aO_2 between 60 and 70 mmHg.** Animals with normal lung function, breathing room air, should have P_aO_2 values >85 mmHg. Increases in inspired oxygen concentration lead to further increases in P_aO_2. A useful clinical rule of thumb is that the P_aO_2 should roughly equal five times the inspired oxygen concentration: an animal on 100% oxygen (anaesthetized and intubated) should have a P_aO_2 of about 500 mmHg, and an animal on 40% oxygen (nasal oxygen or oxygen cage) should have a P_aO_2 of around 200 mmHg. The great majority of oxygen is carried in blood as oxyhaemoglobin, and relatively small amounts are carried as dissolved oxygen. Thus, once the haemoglobin is fully saturated, little overall increase in oxygen delivery to the tissues will occur by dissolving more oxygen in the plasma. If the inspired oxygen concentration has been changed, equilibration to the new P_aO_2 occurs within 2–3 minutes.

P_aO_2 values <75 mmHg are usually treated by oxygen supplementation and addressing the underlying cause of the hypoxaemia. Values <55 mmHg are imminently life-threatening and require immediate action. Decreases in P_aO_2 result from one of the following:

- Decreased oxygen in inspired air (e.g. decreased barometric pressure at high altitudes)
- Hypoventilation (decreased movement of air into the lungs) leading to less availability of oxygen in the alveoli for gas transfer (see below)
- Venous admixture, resulting from:
  - Shunting
  - Ventilation/perfusion mismatch
  - Diffusion impairment.

Shunting implies that a proportion of deoxygenated venous blood completely bypasses functional alveoli. This can occur either by venous–arterial shunts that deliver venous blood directly to the arterial circulation (e.g. reverse patent ductus arteriosus, bronchial anastomoses), or by blood flow to completely non-functional areas of lung, such as severely atelectatic areas or neoplastic masses. In either case, blood with the same oxygen content as systemic venous blood returns to the systemic circulation and mixes with arterial blood, resulting in an overall decrease in P_aO_2. If shunting is the cause of hypoxaemia, the hypoxaemia will not be correctable, no matter how much the inspired oxygen concentration is increased.

The second cause of venous admixture is ventilation/perfusion mismatch. In normal animals, ventilation (the delivery of air to alveoli) and perfusion of the alveoli with blood are fairly closely matched in order to maximize gas transfer. Disease processes such as airway or alveolar disease can change the pattern of ventilation. Similarly, vascular disorders such as thromboembolic disease can change the pattern of perfusion. Significant mismatch of ventilation and perfusion can result, causing hypoxaemia. In such cases, providing an increased inspired oxygen concentration may result in increases in P_aO_2. Ventilation/perfusion mismatch is the most common cause of hypoxaemia in veterinary patients with parenchymal disease.

Diffusion of oxygen across the alveolar capillary membrane may be impaired by any process that leads to thickening of that membrane. As there is a great reserve for diffusion of oxygen, it is unusual for diffusion to be the limiting factor for oxygen transfer, except in very severe disease processes. Since carbon dioxide is about 20 times more soluble than oxygen, diffusion almost never limits carbon dioxide transfer in the lungs.

P_aCO_2 and hypercarbia

The rate of elimination of carbon dioxide from the body directly influences the arterial partial pressure of carbon dioxide (P_aCO_2), whereas the production of carbon dioxide by tissue metabolism is most closely related to venous partial pressure of carbon dioxide (P_vCO_2). Since carbon dioxide is very soluble and has an almost linear dissociation curve, it easily diffuses out of blood into the alveoli, and there is a huge reserve for carbon dioxide elimination from the lung. Thus, P_aCO_2 primarily depends on the extent of ventilation. Minute ventilation is a measure of the total amount of gas moved in and out of the lung per minute, and is a function of respiratory rate and tidal volume. Hyperventilation, such as might occur with fear, pain or pulmonary parenchymal disease, results in low P_aCO_2. Hypoventilation leads to increases in P_aCO_2, and is commonly seen with disorders that affect the mechanical ability to move air into the lungs, and occasionally in animals with severe pulmonary parenchymal disease.

P_aCO_2 values >50 mmHg are significant and require treatment, and values >70 mmHg are imminently life-threatening. P_aCO_2 values <20 mmHg may result in excessive cerebral vasoconstriction and should be treated aggressively. P_vCO_2 can be used to evaluate ventilation,

particularly if the sample has been obtained from a central vein (ideally the vena cava, but jugular samples are often sufficient). The venous CO_2 is normally slightly higher than the arterial CO_2, except in extreme shock states including cardiopulmonary arrest. If P_vCO_2 is elevated, and the sample has been taken from a central vein, hypoventilation is likely to be occurring. If taken from a peripheral vein, then local tissue perfusion and patient struggling can affect the P_vCO_2 and erroneous assumptions can be made about the patient's ventilation status; therefore, hypoventilation must be confirmed using an arterial or central venous blood sample. If the P_vCO_2 is normal or decreased, then the patient is adequately ventilating and no further diagnostic tests are needed.

Increased P_aCO_2 in hypoventilation is accompanied by decreased P_aO_2. In a hypoventilating patient, oxygen supplementation will increase the P_aO_2, but will result in no change in P_aCO_2 values because it does not change the total volume of air moved into and out of the lungs per minute. Examples of the most common causes of hypoventilation include:

- Neurological disease or anaesthesia affecting central medullary respiratory drive
- Spinal cord dysfunction cranial to C4–C5
- Phrenic nerve dysfunction or neuromuscular junction disease
- Chest wall injury
- Respiratory muscle dysfunction
- Airway obstruction.

If P_aCO_2 is high, the animal experiences respiratory distress. Profound respiratory acidosis may result from the hypercarbia, which can become life-threatening by causing decreased cardiac output, hypotension and neurological depression due to carbon dioxide narcosis. Thus, if hypoventilation is found in clinical patients, measures must be taken to improve ventilatory status by addressing the cause of hypoventilation. If correction of the underlying cause is impossible or will take time, PPV support should be considered.

Indices based on oxygen tension

The measured value for P_aO_2 depends on the extent of ventilation and the inspired oxygen concentration, as well as the presence of lung disease. A number of calculations can be performed to allow meaningful comparison between abnormal P_aO_2 values at different ventilation rates and while the patient is receiving oxygen supplementation.

Calculation of the alveolar–arterial oxygen gradient ($P_{A-a}O_2$) gives an estimate of the effectiveness of gas transfer, while removing the variable contribution of the extent of ventilation. As lung dysfunction worsens, the oxygen gradient between the alveoli and the arteries increases. To calculate the gradient, the partial pressure of oxygen in the alveoli (P_AO_2) must first be estimated using the alveolar gas equation:

$$P_AO_2 = F_iO_2 (P_b – P_{H2O}) – P_aCO_2/RQ$$

Where:

- F_iO_2 = the fractional inspired oxygen concentration
- P_b = the barometric pressure
- P_{H2O} = the saturated water vapour pressure at body temperature
- RQ = the respiratory quotient.

At sea level, in room air and assuming RQ for the dog to be about 0.9 on typical diets, the alveolar gas equation can be simplified as:

$$P_AO_2 = 150 – (P_aCO_2)1.1$$

This equation provides a very useful clinical estimate of alveolar PO_2. Measured arterial PO_2 is subtracted from P_AO_2 to give the alveolar–arterial gradient:

$$P_{A-a}O_2 = P_AO_2 – P_aO_2$$

The reference range for $P_{A-a}O_2$ in patients breathing room air is <15 mmHg. Increased gradients are seen in patients with pulmonary parenchymal disease, but the gradient would be expected to be normal in patients with hypoxaemia secondary to pure hypoventilation with no parenchymal lung disease. Calculation of $P_{A-a}O_2$ allows clinical comparison of serial blood gases in patients with variable ventilatory status.

A second clinically useful index based on oxygen tension is the ratio of P_aO_2:F_iO_2. Many arterial blood gases are obtained in critically ill patients that are receiving oxygen supplementation. In such patients, removal of oxygen support in order to obtain arterial samples on room air may be unsafe or inhumane. Calculation of P_aO_2:F_iO_2 ratios allows comparison of serial samples that are obtained at varying concentrations of inspired oxygen. Normal animals usually have a P_aO_2:F_iO_2 >400. Values <200 imply serious lung disease.

Pulse oximetry

Pulse oximetry is used to determine, indirectly, the arterial haemoglobin saturation with oxygen. Oxygen is carried to the tissues attached to haemoglobin in the red blood cells. Each haemoglobin molecule is capable of binding four molecules of oxygen; thus, haemoglobin carries the majority of the oxygen in the blood, with only a relatively small proportion carried as dissolved oxygen in the plasma. The relationship between the P_aO_2 and the amount of oxygen attached to haemoglobin (expressed as % saturation, S_aO_2) is not linear. When one molecule of oxygen binds to haemoglobin, the haemoglobin molecule undergoes a conformational change that allows three more oxygen molecules to bind much more easily. Thus, the oxygen dissolved in the plasma and that carried on the haemoglobin are in fact related by means of a sigmoid curve.

In normal arterial blood, the haemoglobin should be >95% saturated with oxygen. Observation of the curve (see Figure 7.2) demonstrates that the normal animal operates with quite a large safety margin with regard to haemoglobin saturation. Haemoglobin becomes close to fully saturated (>90%) at a P_aO_2 of about 70 mmHg; at this point the curve plateaus and despite higher P_aO_2, haemoglobin saturation (and therefore oxygen transport) cannot be increased much more.

In animals with lung disease, decreases in oxygenation may occur. Once the P_aO_2 becomes as low as 70–75 mmHg (corresponding to an S_aO_2 of 90–92%), the animal comes perilously close to the 'shoulder' of the curve.

The pulse oximeter is a dual wavelength spectrophotometer that measures haemoglobin saturation by transmitting light through a pulsating arterial vascular bed. Transmission of light through tissue is not constant, but varies with each cardiac pulse. The variation in transmitted light is entirely due to arterial blood, with the contribution of venous blood and tissue remaining constant. By using

the appropriate transmitted light wavelengths for oxyhaemoglobin and deoxyhaemoglobin, the microprocessor can continuously calculate oxygen saturation. Pulse oximetry readings of ≥93% are acceptable in non-anaemic critically ill patients breathing room air. Oxygen supplementation should be considered in patients with haemoglobin saturation of <93%. Saturation values of 90% correlate with a P_aO_2 of approximately 60–70 mmHg and indicate severe hypoxaemia. Values <90% should be addressed immediately by providing supplemental oxygen, or treating hypoventilation using reversal of anaesthetic agents or PPV.

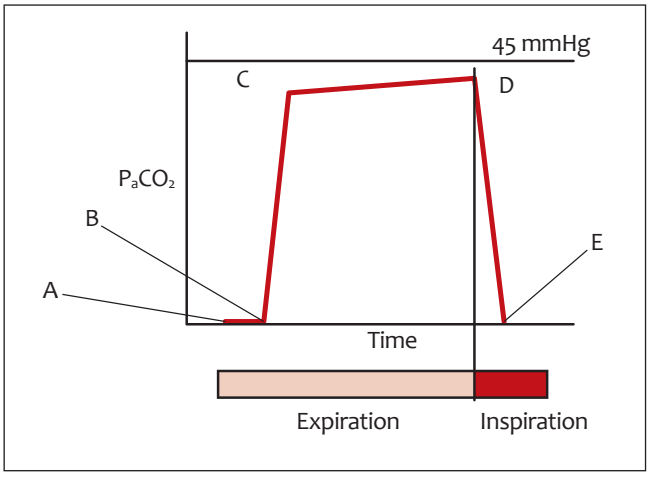
The pulse oximeter has been validated to be accurate in dogs. In awake cats and dogs, the small pulse oximeter probe can be placed on a shaved area of the pinna of the ear, the lip, a fold of skin at the axilla or the inguinal area, or on the prepuce or vulva. In anaesthetized patients, the tongue is the most useful site. The pulse oximeter is non-invasive and very well tolerated by the majority of animals. It provides a continuous read-out of haemoglobin oxygen saturation and pulse rate, thus it is a useful tool for continuous monitoring of the hypoxaemic patient. When arterial blood gas analysis is unavailable, or when arterial blood cannot be obtained, the pulse oximeter can provide a useful indication of arterial saturation and a means of assessing disease progression.

In humans, the accuracy of the pulse oximeter reading has not been noted to change significantly with skin colour, serum quality, or mild to moderate anaemia. However, in dogs, it seems that extremely dark skin pigmentation, as found in Newfoundlands or black Labrador Retrievers, impedes effective pulse oximetry readings. The major limiting factor in the use of pulse oximetry is tissue perfusion. Any condition that diminishes tissue blood flow, such as hypotension or shock, will prevent the pulse oximeter from accurately reading and measuring haemoglobin saturation. Motion of the probe can decrease the ability to obtain a signal, therefore good signals can be difficult to obtain in conscious patients with increased respiratory effort. Ideally, a pulse oximeter that displays a waveform or a heart rate, as well as the simple percentage reading, should be used, as this allows the clinician to make a judgement as to the reliability of the reading. Despite these limitations, the pulse oximeter provides a clinically useful and simple measure of haemoglobin saturation. Newer technology in pulse oximetry, which is now beginning to be clinically available, may help to address some of the limitations relating to poor perfusion and motion artefact.

End-tidal capnography

End-tidal capnography is another indirect technique for respiratory monitoring. The end-tidal capnograph measures the amount of carbon dioxide in exhaled air, and thus can give an indirect estimate of ventilation status. End-tidal carbon dioxide is most frequently measured in anaesthetized and intubated patients. A T-piece is inserted into the system at the end of the endotracheal tube. Some instruments have side-stream ports that aspirate air into the machine, where it is analysed, while others with mainstream ports measure carbon dioxide at the airway. Alternative approaches include placement of the sampling tube at the nares, or its attachment to the end of a tracheostomy tube. The end-tidal capnograph continuously measures the carbon dioxide content of inhaled and exhaled air.

As it is so easily diffusible, the carbon dioxide in pulmonary capillaries equilibrates almost immediately with alveolar air. If carbon dioxide in alveolar air could be measured, it would almost exactly represent that of pulmonary capillary blood. In a single breath, air sampled during inspiration should represent room air and therefore contain virtually no carbon dioxide. As exhalation begins, the air passing the instrument initially represents dead space which has not been in contact with alveolar air. It therefore contains virtually no carbon dioxide. As exhalation continues, alveolar air begins to mix with air from the dead space, with a resultant gradual increase in the amount of carbon dioxide measured by the instrument. Eventually, all the air passing the sampling port is alveolar air, and the partial pressure of carbon dioxide reaches a plateau, which is reported by the instrument as the end-tidal carbon dioxide (Figure 7.40).



7.40 Normal capnogram showing the various phases of respiration. A = baseline, representing the beginning of expiration (dead space gas), this should be zero; B = sharp upstroke, representing the mixing of dead space gas and alveolar gas; C = change to alveolar gas; C–D = the alveolar plateau, increasing towards the endpoint; D = end-tidal carbon dioxide value; E = end of inspiratory phase, showing a rapid decrease in carbon dioxide.
(Courtesy of K Walsh and reproduced from *How to…collected articles from BSAVA Companion 2012–2016*)

Errors in end-tidal carbon dioxide monitoring are primarily related to respiratory rate, especially in panting animals or extremely tachypnoeic patients. Further errors might occur if lung disease results in uneven emptying of alveoli, thus preventing the end-tidal carbon dioxide concentration from reaching a measurable plateau. Another factor to bear in mind when using this type of instrumentation is the volume of air aspirated from the anaesthetic circuit during side-stream monitoring. Instruments in veterinary use aspirate air at a rate of 50–150 ml/min, and anaesthetic gas flow rates should be adjusted accordingly. If this type of instrument is being used with inhalant gas in an anaesthetic circuit, the sampled air should be returned to the circuit or vented to the exterior, rather than allowing release of inhalant gas into the room.

End-tidal carbon dioxide should approximate the venous partial pressure of carbon dioxide, providing an estimate of ventilation status. However, there is usually a variable gradient between the end-tidal result and the venous partial pressure of carbon dioxide. This instrument should therefore be used primarily to follow trends. Normal values should be in the 35–45 mmHg range. If the end-tidal carbon dioxide concentration is >50 mmHg, this result is highly specific for clinically significant hypoventilation, which should be treated immediately.

Intubation and positive pressure ventilation

Extremely dyspnoeic animals that cannot adequately ventilate or oxygenate may require anaesthesia and intubation to establish control over the airway and to provide short-term PPV (Figure 7.41). This aggressive approach is reserved for the most severe cases of respiratory distress, as it is expensive and requires intensive management and some clinical expertise. If PPV is required for more than a few hours, then it is optimal to use specially designed ventilators that provide accurate control over tidal volume, airway pressures, F_iO_2 and humidity. Ventilated animals must be supervised 24 hours a day by qualified clinicians and/or nurses, because frequent and rapid changes in respiratory or cardiovascular function often necessitate minute-by-minute adjustments in ventilator settings.



7.41 Cavalier King Charles Spaniel with severe pulmonary contusions and a pneumothorax following a road traffic accident. He was hypoxaemic and in significant respiratory distress in an oxygen cage, so he was anaesthetized, intubated and positive pressure ventilation was initiated.

Indications for intubation and PPV

Clinical parameters indicating that the animal should be intubated include severe respiratory distress that is non-responsive to therapy, persistent cyanosis that is not responsive to oxygen supplementation or a fractious patient that is not responding to empirical treatment and cannot be restrained for diagnostics or therapy. In any of these situations, anaesthesia eliminates distress and facilitates handling for diagnostic investigation. On blood gas analysis, general indicators for PPV are a P_aO_2 of ≤60 mmHg while the patient is receiving oxygen supplementation, or a P_aCO_2 >50 mmHg that cannot be treated in any other way, e.g. by reversing anaesthetic drugs or by relieving or by-passing an airway obstruction.

Induction of anaesthesia for intubation

Care must be taken when choosing an anaesthetic agent for induction. Often there is concurrent cardiovascular system instability and myocardial irritability due to hypoxaemia. Since the clinician will be establishing control over the airway and taking over respiratory function, concerns about ventilatory depression by anaesthetic agents are reduced. Intravenous anaesthetic agents are ideal because they allow rapid induction, intubation and therefore airway management. Mask induction or the use of intramuscular agents, because of slow onset of anaesthesia, are associated with a high risk of cardiopulmonary arrest when severe respiratory distress is present. If upper airway obstruction is suspected, before inducing anaesthesia the clinician should organize all of the materials required to perform an emergency tracheostomy in the event that endotracheal intubation is not possible (see Figures 7.10 and 7.11).

Where there is no evidence of hypovolaemia, propofol may be administered by intravenous injection to effect, although this drug may be associated with vasodilation and production of intrapulmonary arteriovenous shunting. Shunting may severely aggravate pre-existing hypoxia and, although temporary, is not responsive to increased inspired oxygen concentrations or assisted ventilation. Alternatively, intravenous alfaxalone or low doses of intravenous opioid analgesics, such as fentanyl or morphine, combined with a benzodiazepine sedative agent, such as diazepam or midazolam, may produce adequate sedation and muscle relaxation to allow endotracheal intubation in critically ill patients (see Chapter 21). Respiratory arrest may temporarily occur with the use of opioids, and therefore it is important immediately to intubate and ventilate the patient with 100% oxygen.

Anaesthesia must then be maintained to allow continued intubation using either volatile agent inhalation or repeated administration of injectable drugs. Once the animal has been intubated, it should be immediately placed on 100% oxygen and PPV should be initiated by manually bagging the animal until more information is available about respiratory function. The haemodynamic status of the patient should be carefully monitored, body temperature measured and supported if necessary, and the administration of anaesthetic drugs kept at the minimum required to maintain unconsciousness and lack of response to gentle movement of the endotracheal tube.

Positive pressure ventilation

As it is labour intensive, invasive and associated with numerous complications, PPV in dogs and cats is reserved for severely affected patients when all other treatment possibilities have failed. Hypoxaemia can usually be managed by increasing the concentration of oxygen in inspired air using an oxygen cage, nasal oxygen or mask. If these measures fail, PPV becomes the only option for continued treatment. Similarly, hypoventilation can sometimes be treated by effective management of the underlying problem, but if that fails to result in satisfactory improvement, PPV is required. Patients undergoing PPV require 24-hour nursing and veterinary care and, ideally, a specialized intensive care unit (ICU) ventilator, especially if this type of respiratory support needs to be continued beyond 12–24 hours. Urgent referral to a secondary or tertiary care hospital is usually appropriate for optimal management of these challenging cases.

Ventilator modes

Every part of each breath delivered to the patient by specialized ICU ventilators can be controlled by the operator to select the best options for each individual patient. Specifically, the trigger initiating each breath (and its sensitivity), the pattern of air flow (waveform) during the breath, and the method by which the breath is terminated can all be modified.

Terminating the breath: In volume-limited ventilation, the ventilator is programmed to deliver a given volume of oxygen–air mix, irrespective of the airway pressure that is

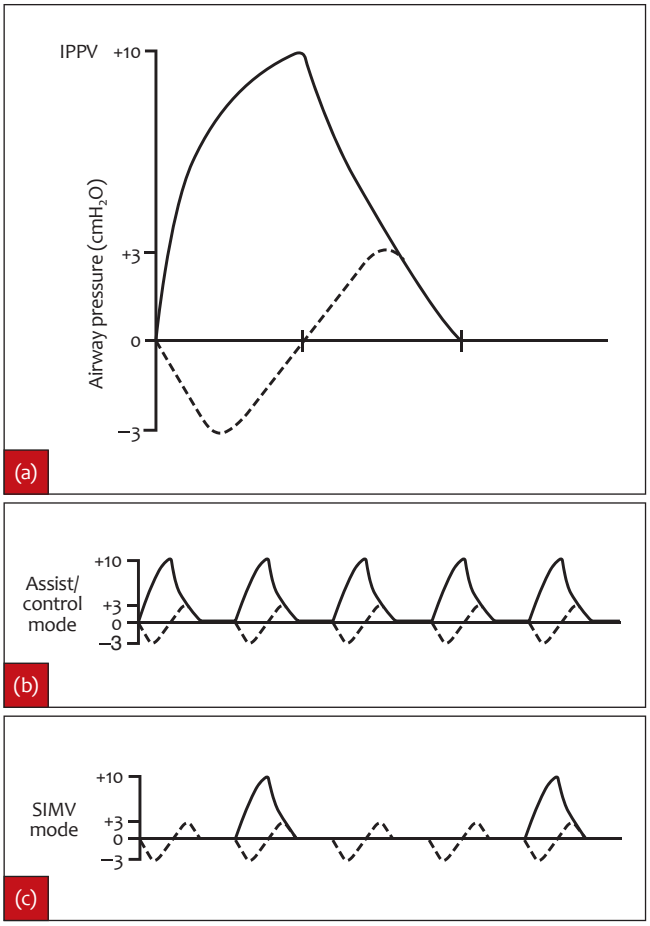
reached. The breath terminates when the desired volume has been delivered. Problems such as mucus plugs in the endotracheal tube or airways are easily detected, as narrowing of the functional airway causes an increase in the peak airway pressure for a given tidal volume.

In pressure-limited ventilation, the ventilator is programmed to deliver oxygen–air up to a given airway pressure, irrespective of the volume delivered. In this mode, tidal volume must be measured frequently, as the presence of lung disease may cause the desired airway pressure to be reached with a smaller than normal tidal volume because of poor lung compliance. Peak pressures vary depending on the requirements of individual patients: animals with very stiff (poorly compliant) lungs may require higher pressures in order to achieve adequate ventilation. However, pressure-limited ventilation is the safest way to ventilate animals with lung disease; by terminating delivery of the breath at a selected peak inspiratory pressure, the lungs can be protected from the barotrauma associated with the delivery of excessively high airway pressures.

Initiating the breath: There are two basic ventilator modes (Figure 7.42) for initiating breath: assist/control (AC) and synchronous intermittent mandatory ventilation (SIMV). The choice of mode depends on the degree of ventilator support that is desired: AC controls ventilation completely with very little effort from the patient; SIMV assists ventilation, but requires varying amounts of patient effort. In the majority of cases AC is used initially, and then the patient is switched to SIMV when it is ready to be weaned from the ventilator.

In AC ventilation, the operator selects a minimum number of breaths that will be delivered per minute. The sensitivity or trigger level of the ventilator can be adjusted so that the machine detects inspiratory efforts by the patient. The breaths are timed to be delivered when the patient creates negative pressure in the airway during inspiration; if the patient is not breathing, the machine will automatically deliver the set minimum respiration rate. If the patient breathes faster than the set rate, the machine is triggered to deliver the desired tidal volume or pressure for each patient-initiated breath, and the display shows a total respiratory rate that is higher than the set rate. Therefore, if the patient is breathing spontaneously, the machine will deliver a full breath for every patient-initiated breath. This results in the ventilator performing almost all of the work of breathing in this mode. This mode can become problematic in patients with a rapid and shallow respiratory rate; hyperventilation can result, as each breath taken by the patient results in delivery of a full tidal volume.

In SIMV, the ventilator is set to deliver a desired minimum number of breaths per minute, just as in AC. The breaths are delivered when the machine senses a negative pressure effort by the patient ('synchronous'). Between each breath, if the patient breathes spontaneously, the machine does not 'kick in' with additional help, and these spontaneous breaths reach a tidal volume that is determined by the patient. This causes the animal to perform a varying proportion of the work of respiration on its own. The set minimum number of breaths per minute can gradually be decreased, allowing for more spontaneous ventilation, and therefore gradually increasing the respiratory work by the patient. Thus, this mode of ventilation is very useful for weaning from the ventilator, and is also useful for patients with rapid, shallow respiratory patterns, as it prevents the hyperventilation mentioned above with the AC mode.



7.42 (a) A ventilator breath compared with a spontaneous patient breath. The spontaneous breath (dotted line) begins as a negative inspiratory effort, followed by a slightly positive airway pressure during exhalation. In contrast, the ventilator breath (solid line) generates exclusively positive airway pressure. (b) In assist/control ventilation, the ventilator delivers a set number of breaths, to a set pressure or tidal volume. The machine delivers these breaths when the patient creates a negative pressure in the airway; if the patient is not breathing, the machine will automatically deliver the set respiration rate. If the patient breathes faster than the set rate, the machine is also triggered, and it will deliver the desired tidal volume for each patient-initiated breath. (c) In synchronous intermittent mandatory ventilation (SIMV), the ventilator is set to deliver a desired number of breaths. The breaths are delivered when the machine senses a negative pressure effort by the patient ('synchronous'). Between each breath, if the patient breathes spontaneously, the machine does not 'kick in' with a breath of its own, and these patient-induced breaths only reach the negative pressure and tidal volume determined by the patient.
IPPV = intermittent positive ressure ventilation.

Positive end-expiratory pressure

Positive end-expiratory pressure (PEEP) can be used to improve oxygenation in the intubated hypoxaemic patient. It should be used for hypoxaemic animals that are being adequately ventilated based on P_aCO_2 levels, but remain hypoxaemic in spite of oxygen supplementation. By applying small amounts of positive pressure to the airway, complete expiration is prevented, resulting in:

- Increased functional residual capacity
- Increased alveolar size and recruitment
- Prevention of early closure of small airways.

This can sometimes lead to marked improvement of oxygenation, particularly in animals with pulmonary oedema or haemorrhage. It usually does not significantly affect carbon dioxide. However, it is not without its drawbacks;

high levels of PEEP decrease venous return to the heart, increase central venous pressure and increase the mechanical work of breathing. The use of PEEP to improve oxygenation sometimes allows decreases in the concentration of inspired oxygen. This can be particularly useful in animals that are being ventilated with very high oxygen concentrations and, thus, are at risk of oxygen toxicity. PEEP should be started at 5 cm H_2O and slowly increased until the desired endpoint in terms of improvement in oxygenation is reached. It is important to watch haemodynamic variables closely as PEEP is increased, since it may lead to increased incidence of cardiovascular instability.

Goals of ventilation

The aim should be to maintain the P_aO_2 at 80–100 mmHg or higher, and to keep the P_aCO_2 between 30 and 45 mmHg, depending on the condition of the animal, its acid–base status, and whether or not efforts are being made to wean the animal from the ventilator. P_aCO_2 should be at the lower end of the range in animals with cerebral oedema or head trauma or in animals that have severe metabolic acidosis. The P_aCO_2 is adjusted to the desired level by manipulation of the respiratory rate and tidal volume. P_aO_2 achieved in the ventilated animal depends on:

- Extent of lung disease
- The concentration of oxygen
- Ventilation rate, tidal volume and peak inspiratory pressure
- The use of PEEP.

General recommendations suggest that during PPV, peak airway pressures of 10–20 cm H_2O should be the goal. The respiratory rate should be set between 10 and 30 breaths per minute, depending on the severity of lung disease; the inspiratory to expiratory ratio should be approximately 1:2 or 1:3. F_iO_2 should be set at 100% to start, then rapidly weaned to the lowest possible level depending on oxygen saturation.

In animals with normal lungs, the low end of the desired airway pressure range will usually be achieved if the patient is ventilated with tidal volumes of 8–12 ml/kg. Numerous studies have confirmed adverse effects in the lungs if airway pressures exceed 30 cm H_2O, including alveolar inflammation, rupture of alveolar septae, emphysema and pneumothorax. In contrast to normal lungs, the diseased lung can be very heterogeneous. Lung units with normal alveoli may be located side-by-side with abnormal lung units. PPV with normal tidal volumes can result in very high peak airway pressures and over-distension of normal alveoli, which accept a relatively large proportion of the delivered breath because they are more compliant in comparison with the diseased alveoli, which may not fill with gas. Over-distension of the normal alveoli results in alveolar inflammation. Pneumothorax is the most dramatic and easily recognized complication of barotrauma and volutrauma in the ventilated patient.

In addition, some alveoli and terminal bronchioles may be 'recruitable' (i.e. collapsed at end expiration but expanded during inspiration). In these recruitable alveoli and the alveoli immediately adjacent to them, lung injury and inflammation may occur due to shear stress as they are opened and then collapse completely with each breath. By applying PEEP, the recruitable alveoli are held open at the end of exhalation, thereby minimizing additional inflammation caused by shear stress. Multiple recent studies suggest that lung-protective ventilation strategies may result in decreased lung inflammation and improved survival. High levels of PEEP are used to recruit alveoli and increase functional residual capacity, thereby preventing the cycle of alveolar reopening and stretching with each breath. Current recommendations suggest that tidal volumes and peak airway pressures should be kept as low as possible (ideally 6–8 ml/kg and <30 cm H_2O, respectively) in order to prevent over-distension of relatively normal alveoli and shear stress. Increased physiological and anatomical dead space and low tidal volumes can result in problems with carbon dioxide elimination during PPV, particularly at low tidal volumes. The term 'permissive hypercapnia' refers to acceptance of a higher than normal P_aCO_2 (as long as respiratory acidosis is not severe), in order to minimize tidal volumes and airway pressures.

Complications of PPV

Animals being managed with PPV are at a high risk of developing pneumonia because airway intubation bypasses upper airway defences, atelectasis predisposes to impaired bacterial clearance from the alveoli, and there are often increased populations of resistant Gram-negative bacteria in the oropharynx, especially if the animal is receiving antibiotics or H2 blockers. In addition, most critically ill ventilator patients can be expected to be immunocompromised because of their illness, the need for long periods of general anaesthesia, and often decreased nutrition. Pneumonia is a potentially serious complication in the ventilated patient because it predisposes to sepsis and worsening of SIRS, as well as multiple organ failure. In addition, it can lead to progressive worsening of hypoxia and delay of weaning, and therefore can potentially contribute to mortality. Ideally, surveillance bacterial cultures should be submitted daily from the airway. The use of prophylactic antibiotics is not generally considered ideal; the optimal approach is to diagnose infection as early as possible, and to initiate targeted therapy at that time. If there is clinical evidence of pneumonia, broad-spectrum antibiotic therapy should be administered immediately, pending the result of bacterial cultures.

Monitoring the ventilated patient

Blood gases should be measured at least every 6 hours, in order to assess progress and monitor for deterioration in pulmonary function or changes in acid–base status. The ventilator settings should be adjusted based on these results. Packed cell volume, total solids/protein and serum electrolytes should be measured at least every 6 hours, and abnormalities corrected. Continuous monitoring of oxygen saturation using a pulse oximeter will give warning if the animal suddenly desaturates. End-tidal carbon dioxide can be monitored, providing an estimation of the P_aCO_2, and can therefore be used to adjust the ventilation volumes and pressures.

The endotracheal tube should be aspirated daily and cytology and culture performed on the aspirates. The ventilated animal should have frequent chest radiographs to monitor for deterioration or improvement. Ideally chest radiographs should be obtained daily, but they are indicated if there is any deterioration of the clinical condition of the animal.

Continuous electrocardiographic monitoring is necessary to monitor heart rate and for the presence of dysrhythmias. Arterial pressure should be monitored frequently, ideally using continuous direct arterial monitoring via an arterial catheter, which is also useful for obtaining

regular blood gases. Hypotension should be treated as required. Urine output should be monitored and should be at least 1–2 ml/kg/h. Body temperature should be monitored and heat support provided as needed.

Outcomes of PPV

The successful outcome of PPV is defined as weaning the patient from the ventilator and their subsequent discharge from hospital. Although outcomes continue to improve, the selection of only the very sickest patients for this type of support means that overall survival rates are lower than preferred. Pet owners should be educated about the expense of PPV and the extensive resources (equipment, staff expertise) needed for a positive outcome.

The literature includes numerous case reports of individual animals successfully managed using PPV (Aldrich *et al*., 2002; Kelmer *et al*., 2012; Guillamin and Hopper, 2013; Allen *et al*., 2016); however, it is important to examine the results in terms of groups of relevant patients, in order to gain the best perspective on survival expectations. Patients that require PPV can be divided into two general categories that differ greatly in regard to the success of weaning and discharge.

- Animals that require PPV because of ventilatory failure but have normal lungs – these patients are generally easier to manage and have better outcomes.
- Animals that require PPV because of lung disease (i.e. a failure of oxygenation) – these patients tend to be difficult to manage and have much lower rates of survival to discharge.

Furthermore, there is variability within these two groups depending on the underlying disease and bodyweight of the animal. Smaller animals tend to have worse outcomes, regardless of the reason for PPV. This is particularly true of cats, which have lower survival rates than dogs across all disease processes, should they require PPV.

Patients with ventilatory failure: Animals that require PPV because of ventilatory failure include those with brain, spinal cord or neuromuscular disease, chest wall abnormalities and airway obstructions. Typically, these animals have normal lungs, at least at the onset of PPV. Thus, they are relatively easy to support on the ventilator. Outcomes often depend on the underlying disease process. For example, a cat that requires PPV because of cerebral oedema due to an inoperable brain tumour is likely to have a worse prognosis than a large dog that requires PPV following cervical spinal cord compression surgery.

Published overall outcomes in this category report survival to discharge rates of 35–60% (King and Boothe, 1994; Drellich, 2002; Hopper *et al*., 2007). However, outcomes in specific sub-groups within this category may be higher or lower. For example, the survival to discharge rate in a group of 14 dogs that required PPV because of cervical spinal cord injury was 70% in one study (Beal *et al*., 2001). In contrast, a large study of cats managed with PPV reported a 33% survival rate (Lee *et al*., 2005), and another study reported a 21% survival to discharge rate (3/14) in a group of dogs ventilated to manage lower motor neuron disease (Rutter *et al*., 2011).

Patients with oxygenation failure: Survival rates are much lower in animals that require PPV because of severe lung disease. Common examples of this type of case include patients with pneumonia, pulmonary oedema, pulmonary haemorrhage, pulmonary thromboembolism or ARDS. In these animals, PPV is difficult because of the need to provide sufficient oxygenation and removal of carbon dioxide without causing additional ventilator-induced lung injury. Further challenges with these patients include the high risk of SIRS and subsequent organ failure, which might result in mortality independent of the lung disease.

Published overall outcomes in this category report survival to discharge rates of 11–22% (King *et al*., 1994; Drellich, 2002; Hopper *et al*., 2007). However, the survival rates for specific subgroups within this category may differ from this range. One study reported 30% survival in a group of dogs managed with PPV for severe pulmonary contusions following trauma (Campbell and King, 2000). As expected, the outcomes for this subset of cats were worse than those for dogs, with reported survival rates of 14% in one study (Lee *et al*., 2005).

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Chapter 8

Renal and urinary tract emergencies

Jonathan D. Foster and Karen Humm

The renal and urinary tract system is vital for the maintenance of electrolyte, acid–base and fluid balance. Disturbance of its function therefore results in homeostatic derangement, potentially leading to severe illness and even death. Possible causes of renal or urinary tract dysfunction range from toxin ingestion to trauma to feline lower urinary tract disease. This chapter addresses common renal and urinary tract emergencies and the approach to their management.

Identification of renal or urinary tract dysfunction

Azotaemia

Detection of azotaemia is often the first step in the recognition of renal or urinary tract dysfunction. Azotaemia is defined as an increase in nitrogenous compounds in the blood, generally identified by raised urea and creatinine levels. These products are excreted by the kidneys and so azotaemia is a useful indicator of renal or urinary tract pathology. It is important to determine whether the azotaemia is of pre-renal, renal (intrinsic) or post-renal origin (Figure 8.1). In some cases this will rapidly become apparent during physical examination or history taking, but further investigation involving urinalysis, additional blood testing or diagnostic imaging may be required.

Azotaemia does not develop until there is loss of at least 75% of renal function, however, and so it is not a very sensitive indicator of intrinsic renal disease. Isosthenuria is a slightly more sensitive indicator of renal dysfunction, developing when there is at least 66% loss of renal function. However, this is still suboptimal when attempting to identify renal injury and (together with the lack of a clear definition for acute renal failure) has led to the development of new criteria defining 'acute kidney injury' in humans, which have now been adopted in small animal medicine.

Acute kidney injury

In human nephrology, the term acute kidney injury (AKI) has supplanted the use of acute renal failure. AKI is preferred because it draws attention to small insults that affect renal function but do not cause overt failure, as well as introducing concepts of maintenance and recovery from the inciting injury. AKI can refer to any loss of renal function; however, it is most commonly applied to loss of tubular function. Additionally, it has been shown in human medicine that mild decreases in glomerular filtration rate (GFR), as observed through serial assessment of serum creatinine, may be associated with adverse clinical outcomes, without patients necessarily developing azotaemia (Chertow, 2005).

Parameter	Pre-renal (intrinsic)	Renal	Post-renal
Urine specific gravity	Hypersthenuric (>1.040 in cats and >1.030 in dogs) unless complicating disease is present, e.g. hypoadrenocorticism, hypercalcaemia, *Escherichia coli* sepsis	Variable depending on stage of disease but often isosthenuric (1.008–1.012) or poorly concentrated (<1.025)	Variable
Dipstick results		Glucosuria and proteinuria common	
Sediment examination	Generally unremarkable	Casts, erythrocytes, bacteria, leucocytes and/or neoplastic cells may be seen	Erythrocytes common
Bladder size	Generally small	Variable depending on stage of disease process	Either large and tense or absent
Diagnostic imaging	Kidneys and urinary tract unremarkable	Renomegaly and ultrasonographic changes possible. Small kidneys seen if the azotaemia is chronic	Possible abnormalities include: • Reno-, uretero-, cysto- or urethroliths • Ureteral dilatation • Free abdominal fluid • Contrast studies may reveal urinary tract rupture or obstruction

8.1 Criteria used to differentiate between pre-renal, renal and post-renal causes of azotaemia.

AKI has four phases:

- **Induction phase:** this begins with the ischaemic or nephrotoxic insult, and continues until there is a change in renal function, such as decreased urine output or an increased urea or creatinine level. The length of time necessary to see changes is variable and depends on the nature and severity of the insult. During this stage, early intervention may prevent progression; clinical signs are often not apparent, which makes intervention difficult, but anticipation of the risk of AKI and careful monitoring of renal function is beneficial in at-risk patients
- **Extension phase:** the kidney is further injured by alterations in renal perfusion, continued hypoxia, secondary inflammation, and ongoing epithelial and endothelial injury
- **Maintenance phase:** this occurs after a critical amount of damage is established. The resulting decreased GFR results in azotaemia and clinical signs of uraemia, especially if combined with ongoing renal hypoperfusion. Elimination of inciting factors at this phase will not decrease existing damage or expedite the rate of recovery. This phase may last from days to weeks
- **Recovery phase:** this is the period where renal tissue undergoes regeneration and repair with varying restoration of renal function.

AKI may occur secondary to pre-renal, post-renal and/or intrinsic renal causes. Recently, the International Renal Interest Society (IRIS, www.iris-kidney.com) has adopted a stratification scheme for veterinary AKI (Figure 8.2) which allows categorization of the severity of injury, aids therapeutic decision-making, and provides a means of classification for research and collaborative efforts. The severity of injury increases along with the IRIS AKI Grade. Note that IRIS AKI Grade I includes serum creatinine values that fall within the reference interval for most veterinary chemistry analysers, thus highlighting the need for monitoring trends in laboratory parameters. An increase in serum creatinine ≥26.4 μmol/l within 48 hours would represent AKI, and efforts should be made to determine the cause (e.g. hypovolaemia/dehydration/hypoperfusion, tubular injury).

Proteinuria

Proteinuria may also indicate renal dysfunction. Similar to azotaemia, pre-renal, post-renal and intrinsic renal causes should be considered. Pre-renal causes of proteinuria include Bence Jones proteinuria, haemolysis and rhabdomyolysis; post-renal causes include cystitis, prostatitis, vaginitis and neoplasia. The renal origin of proteinuria can be glomerular (resulting from abnormal permselectivity of the glomerular filtration barrier) or tubular (caused by failure of tubular protein reabsorption or damage to the tubular epithelium). After pre- and post-renal causes of proteinuria have been excluded, the magnitude of proteinuria should be evaluated by a urine protein:creatinine ratio (UPC). The severity of increased UPC cannot be used to differentiate tubular and glomerular origins of proteinuria, nor can it be used to suggest the type of glomerulopathy present (e.g. amyloidosis, immune complex glomerulonephritis, non-immune complex glomerulonephritis). Proteinuria may cause oxidative damage to the tubular epithelium, resulting in AKI. The nephrotic syndrome (proteinuria, hypoalbuminaemia, ascites/oedema and hypercholesterolaemia) may be present. In addition to albumin, antithrombin may be lost via the urine, resulting in a hypercoagulable state. Serum albumin concentration cannot be used to predict antithrombin deficiency; antithrombin activity needs to be measured directly. Complications of proteinuria can include thromboembolism, systemic hypertension and reduced tolerance towards intravenous crystalloid therapy.

Emergency management of the acute kidney injury patient

Most patients with azotaemia (whether pre-renal, intrinsic or post-renal) require stabilization to prevent worsening of the kidney injury and progression to intrinsic AKI. It is important to rapidly assess the patient's perfusion status and address hypovolaemia or dehydration with fluid therapy (see Chapter 4) to improve renal perfusion. In addition, fluid therapy often leads to the correction or improvement of electrolyte and acid–base disturbances, particularly if they are mild, and therefore specific therapy to treat electrolyte and acid–base abnormalities can be withheld in many cases until the effect of fluid therapy is seen. An exception to this is severe symptomatic hyperkalaemia. Hyperkalaemia is a common electrolyte disturbance in AKI patients, potentially leading to bradycardia and arrhythmias, and may require rapid treatment if the effects are marked. The patient's cardiovascular system should be

AKI grade	Serum creatinine	Clinical description
Grade I	<140 μmol/l (<1.6 mg/dl)	**Non-azotaemic AKI:** a. Documented AKI (historical, clinical, laboratory or imaging evidence of AKI, clinical oliguria/anuria, volume responsiveness[a]) and/or b. Progressive non-azotaemic increase in serum creatinine; ≥26.4 μmol/l (≥0.3 mg/dl) within 48 hours c. Measured oliguria (<1 ml/kg/h) or anuria over 6 hours
Grade II	141–220 μmol/l (1.7–2.5 mg/dl)	**Mild AKI:** a. Documented AKI and static or progressive azotaemia b. Progressive azotaemic increase in serum creatinine; ≥26.4 μmol/l (≥0.3 mg/dl) within 48 hours, or volume responsiveness[a] c. Measured oliguria (<1 ml/kg/h) or anuria over 6 hours
Grade III	221–439 μmol/l (2.6–5.0 mg/dl)	**Moderate to severe AKI:** a. Documented AKI and increasing severities of azotaemia and functional renal failure
Grade IV	440–880 μmol/l (5.1–10.0 mg/dl)	
Grade V	>880 μmol/l (>10.0 mg/dl)	
Each grade of AKI is further subdivided on the basis of: 1. Non-oliguric or oligoanuric 2. Requirement for renal replacement therapy		

8.2 International Renal Interest Society (IRIS) AKI grading criteria. [a]Volume responsive is considered to be an increase in urine production to >1 ml/kg/h over 6 hours and/or a decrease in serum creatinine to baseline over 48 hours.

carefully assessed to decide whether calcium gluconate therapy is required. (See Chapter 5 for more details on the management of hyperkalaemia.)

Other electrolyte disturbances such as high or low values for sodium, chloride, phosphate or calcium may occur but are less likely to require specific therapy. The need for specific therapy for these disturbances should be decided upon but this can be considered after fluid therapy has been initiated (see Chapter 5).

Metabolic acidosis is very common in the AKI patient. This does not generally require treatment in patients with pre-renal and post-renal causes of AKI if the underlying cause can be fairly rapidly controlled. However, in the intrinsic AKI patient with severe metabolic acidosis (a pH <7.15), bicarbonate therapy may be necessary (see Chapter 5).

If a toxic cause is known or suspected for AKI, decontamination should be performed and any known antidote administered. In any AKI patient it is extremely important to avoid any nephrotoxic drugs, such as non-steroidal anti-inflammatory drugs (NSAIDs) or radiopaque contrast agents. Agents that cause hypotension, including most general anaesthetics and many sedative agents, will decrease GFR and so should also be avoided if possible. The patient's blood pressure should be measured, as hypotension can be seen in hypovolaemic patients or those with other causes of hypoperfusion, and hypertension can occur secondary to AKI or as a cause of AKI. Both conditions require prompt treatment, as they can exacerbate AKI and can also lead to damage to other organs.

Finally, in many patients with AKI the placement of a urethral catheter (Figures 8.3 to 8.8) can be very helpful to allow assessment of urine output and specific gravity, as well as potentially aiding treatment of the underlying disease process in post-renal AKI. Urethral catheterization can also prevent urine scalding and discomfort in polyuric or immobile patients, thus improving their welfare. Appropriate urine output and specific gravity of urine will vary dependent on the underlying disease process causing AKI, but in patients with intrinsic AKI which have been appropriately volume resuscitated and rehydrated, a urine output of less than 2 ml/kg/h would be considered oliguric.



8.4 Retraction of the prepuce of a male cat to aid placement of a urethral catheter



8.5 A closed urine collection system.

- Sedation is generally required unless the patient is paralysed or moribund.
- Place the cat in lateral recumbency.
- Clip and aseptically prepare the perineal area.
- Aseptically prepare hands and wear sterile gloves.
- A silicone-coated urinary catheter is less irritant than polypropylene. Open-ended catheters (rather than those with side openings) allow easier flushing. Sterile lubricant should be placed on the end of the catheter.
- Retract the prepuce and hold in place cranially between the forefinger and thumb of the non-dominant hand (this can be performed by an assistant; see Figure 8.4).
- Place the tip of the urinary catheter into the urethra and gently advance approximately 0.5 cm. If you are unable to place the catheter into the tip of the urethra, gently massage the tip of the penis; occasionally there is a mucoid plug right at the tip which prevents placement.
- If any resistance is noted then flush the catheter with sterile saline.
- Once the catheter is in the urethra, allow the prepuce to return to its resting position and then gently pull the prepuce caudally. This allows alignment of the penile and membranous urethrae and thereby eases passage of the catheter.
- Advance the catheter gently, flushing with sterile saline if any resistance is encountered. Gentle rotation of the catheter may aid advancement.
- Once the catheter is in the bladder, suture the catheter to the perineal region. Drain urine from the bladder using a syringe, taking any samples required.
- If the cat was suffering from urethral obstruction then flush the bladder with warmed sterile saline until the fluid draining is no longer sanguineous.
- Attach a collection bag (a dry, clean, empty fluid bag and giving set is acceptable if a purpose-designed bag is not available) to the urinary catheter and tape the catheter to the cat's tail to decrease any drag on the perineum and penis.
- Place the collection bag on a clean incontinence pad on the floor (see Figure 8.5) or hook to a kennel door lower than the patient to allow free urine drainage.
- Alternatively, bung the urinary catheter.
- **DO NOT** leave the urinary catheter open.
- Drain urine in a sterile fashion every 4 hours and record the volume produced.
- Place an Elizabethan collar on the cat.

8.3 Urethral catheterization of the male cat.

- Sedation is generally required unless the patient is paralysed or moribund.
- Place the cat in lateral or sternal recumbency.
- Clip and aseptically prepare the perineal area.
- Aseptically prepare hands and wear sterile gloves.
- A silicone-coated urinary catheter is less irritant than polypropylene. Sterile lubricant should be placed on the end of the catheter.
- A stylet, or storage of catheters in the freezer, can increase catheter rigidity, aiding placement.
- To place the catheter in a blind fashion pull the vulval lips caudally with the non-dominant hand and advance the catheter ventrally along the vestibular floor in the midline, and it should enter the depression on the vaginal floor into the external urethral orifice.
- Alternatively, a sterilized otoscope head can be used to visualize the external urethral orifice.
- The catheter can then be sutured to the perineum.
- Attach a collection bag (a dry, clean, empty fluid bag and giving set is acceptable if a purpose-designed bag is not available) to the urinary catheter and tape the catheter to the cat's tail to decrease any drag on the perineum.
- Place the collection bag on a clean incontinence pad on the floor (see Figure 8.5) or hook to a kennel door lower than the patient to allow free urine drainage.
- Alternatively, bung the urinary catheter.
- **DO NOT** leave the urinary catheter open.
- Drain urine in a sterile fashion every 4 hours and record the volume produced.
- Place an Elizabethan collar on the cat.

8.6 Urethral catheterization of the female cat.

- Sedation is not required unless the dog is suffering from urethral obstruction or is extremely nervous, aggressive or excitable. Generally, calm firm restraint is sufficient.
- Gently restrain the dog in lateral recumbency.
- Clip long hairs at the end of the prepuce if present.
- Aseptically prepare hands and wear sterile gloves.
- An assistant should extrude the penis by retracting the prepuce and placing pressure at the base of the penis.
- The penis should be cleaned with dilute chlorhexidine.
- A stiff polypropylene catheter is most appropriate if catheterization is being attempted in a patient with urethral obstruction. For long-term placement a soft silicone Foley catheter is more appropriate as it is less irritant and does not require suturing in place.
- Sterile lubricant should be placed on the end of the catheter.
- The catheter should be inserted into the urethral opening and gently advanced; the non-dominant hand is generally required to hold the penis steady as the tip can be very mobile.
- Once in the urethra, the catheter should be gently advanced.
- In a patient with urethral obstruction, if resistance is noted then the catheter should be flushed with sterile saline.
- If this fails to allow progression of the catheter then retropulsion can be attempted. An assistant places a finger in the rectum and compresses the pelvic urethra ventrally against the pelvis. Sterile saline is then injected until some pressure builds up in the urethra. The assistant then lifts their finger, removing the compression and hopefully allowing flushing of any urethrolith into the bladder. In most cases the patient will require sedation or general anaesthesia for this procedure to be performed, which will also aid muscular relaxation of the urethra.
- Once the catheter is in the bladder, urine should flow freely. Foley catheters should be advanced the entire length before the bulb is inflated to prevent inflation in the urethra and consequent trauma. The Foley bulb should be slowly inflated with the designated volume of sterile saline. The catheter can then be gently pulled out of the urethra until there is resistance felt when the Foley bulb is in the neck of the bladder.
- If a polypropylene catheter has been used to retropulse urethroliths into the bladder, this can be removed and a Foley catheter placed (this may not be possible if urethroliths are still present in the urethra and the polypropylene catheter bypassed them. In this case the catheter should be sutured in place).
- Drain urine from the bladder using a syringe, taking any samples required.
- Attach a collection bag (a dry, clean, empty fluid bag and giving set is acceptable if a purpose-designed bag is not available) to the urinary catheter.
- Place the collection bag on a clean incontinence pad on the floor (see Figure 8.5) or hook to a kennel door lower than the patient to allow free urine drainage.
- Alternatively, bung the urinary catheter.
- 19. **DO NOT** leave the urinary catheter open.
- Drain urine in a sterile fashion every 4 hours and record the volume produced and specific gravity.
- An Elizabethan collar may be required in some patients.

8.7 Urethral catheterization of the male dog.

Urethral catheterization of the bitch can be performed via a blind technique or with the use of a speculum. Although both are possible in the moribund conscious dog, sedation is generally required for blind placement, and sedation or anaesthesia is almost always required for placement with the aid of a speculum.

Blind catheterization

- Gently restrain the dog in lateral or sternal recumbency.
- Clip any long hair in the region of the vulva if present and clean the area with dilute chlorhexidine.
- Aseptically prepare hands and wear sterile gloves.
- A stiff polypropylene catheter is most appropriate if catheterization is being attempted in a patient with urethral obstruction. For long-term placement a soft silicone Foley catheter is more appropriate as it is less irritant and does not require suturing in place.
- The use of a guidewire can be very helpful in directing a Foley catheter into the urethral orifice.
- Sterile lubricant should be placed on the end of the catheter.
- Gently introduce the index finger (a smaller finger may be required in very small bitches) of the non-dominant hand into the vestibule.
- Advance into the vestibule and palpate along the ventral floor to locate the external urethral orifice, which is just caudal to the urethral papilla (palpable as a slight bulge of the mucosa).
- With the dominant hand, gently advance the catheter, which should be guided ventral to the non-dominant index finger.
- Once in the urethra, the catheter should be gently advanced.

8.8 Urethral catheterization of the bitch. (continues) ▶

Blind catheterization *continued*

- Once the catheter is in the bladder, urine should flow freely. Foley catheters should be advanced the entire length before the bulb is inflated to prevent inflation in the urethra and consequent trauma. The Foley bulb should be slowly inflated with the designated volume of sterile saline. The catheter can then be gently pulled out of the urethra until there is resistance felt when the Foley bulb is in the neck of the bladder.
- Drain urine from the bladder using a syringe, taking any samples required.
- Attach a collection bag (a dry, clean, empty fluid bag and giving set is acceptable if a purpose-designed bag is not available) to the urinary catheter.
- Place the collection bag on a clean incontinence pad on the floor (see Figure 8.5) or hook to a kennel door lower than the patient to allow free urine drainage.
- Alternatively, bung the urinary catheter.
- **DO NOT** leave the urinary catheter open.
- Drain urine in a sterile fashion every 4 hours and record the volume produced and specific gravity.
- An Elizabethan collar may be required in some patients.

Visually guided catheterization

- Place the dog in dorsal recumbency with the legs pulled cranially, in sternal recumbency with the legs hanging down from the edge of the table or in lateral recumbency with the legs pulled forward.
- Prepare the patient, clinician and catheter as described above (first six points).
- Lubricate a vaginal speculum with sterile lubricant.
- Introduce the speculum into the vulva and gently direct dorsally and cranially into the vestibule.
- A light source aids visualization of the external urethral orifice, which is located midline in the cranial ventral vestibule.
- Introduce the catheter into the urethral orifice under direct visualization and then follow the tenth to seventeenth points above.

8.8 (continued) Urethral catheterization of the bitch.

Pre-renal azotaemia

Pre-renal azotaemia results from inadequate renal perfusion preventing effective excretion of nitrogenous waste. The kidneys will function if adequately perfused, generally allowing a rapid and simple resolution of the azotaemia once renal blood flow is restored. However, if renal perfusion is impaired for a prolonged period, renal hypoxia can lead to acute tubular necrosis and the development of intrinsic AKI. Therefore, it is important to recognize patients with pre-renal azotaemia promptly and treat them effectively. Dehydration or hypoperfusion (see Chapters 3 and 4) are the most common causes of pre-renal azotaemia in cats and dogs – i.e. there is inadequate fluid intake compared with losses (both normal and abnormal). Chapter 4 describes the physical examination findings expected in hypovolaemic and dehydrated patients. Common underlying causes are listed in Figure 8.9.

Cause of decreased renal perfusion	Examples
Loss of circulating volume	• Gastrointestinal (vomiting and diarrhoea)[a] • Ascites[a] • Blood loss[a] • Heatstroke • Pleural fluid • Polyuria[a] • Burns • Diuretic use[a]
Decreased intake of fluid	• Inadequate water intake (more common with increased water demand, e.g. chronic kidney disease patients)[a]
Decreased cardiac output	• Cardiac failure (often worsened by diuretic and ACE inhibitor use)[a] • Obstructive shock • Dysrhythmias
Vasodilation	• Distributive shock • Anaphylaxis • Anaesthetic drugs • Positive pressure ventilation • Vasodilator therapy
Hyperviscosity	• Polycythaemia • Hyperproteinaemia/hyperglobulinaemia
Decreased renal blood flow	• Thromboembolism

8.9 Causes of pre-renal azotaemia. [a] Indicates the most common causes. ACE = angiotensin-converting enzyme.

The simplest way to differentiate a pre-renal from a renal azotaemia is to measure urine specific gravity using a refractometer. Cystocentesis is a straightforward procedure to perform in both cats and dogs (described in Figure 8.10), allowing a urine sample to be obtained quickly. Patients with a pre-renal azotaemia and normal renal function without prior administration of fluids or diuretics would be expected to have an elevated urine specific gravity, whereas patients with a renal azotaemia have inadequately concentrated urine (urine specific gravity between 1.008 and 1.025). However, the clinician should be aware that several diseases prevent appropriate concentration of urine in the face of decreased renal perfusion, despite adequate renal function. Hypoadrenocorticism, hypercalcaemia and *Escherichia coli* sepsis can all cause pre-renal azotaemia in conjunction with isosthenuric urine, due to the primary disease interfering with renal urine concentrating mechanisms. This is important as the azotaemia in these patients could be mistakenly attributed to intrinsic renal disease,

Cystocentesis can be performed blind or with ultrasound guidance. Ultrasound guidance is preferred in animals where the bladder is not palpable, for example in small or obese patients.

- The patient should be firmly but gently restrained. It can be standing or in lateral or dorsal recumbency as preferred by the clinician.
- If a sterile sample is required, the patient should be clipped and the skin aseptically prepared over the region where the needle is to be introduced.
- A 21 or 23 G needle of appropriate length to pass through the body wall should be attached to a syringe.
- If ultrasound guidance is being used, the bladder should be identified. The needle should then be introduced into the bladder and the urine aspirated. The needle should be visible ultrasonographically. To achieve this, the needle should be kept in the same plane as the ultrasound probe and the needle introduced adjacent to the probe.
- If cystocentesis is being performed without ultrasound guidance, the bladder should be palpated and then pushed caudally and stabilized with the non-dominant hand.
- If the patient is in dorsal recumbency, the needle should be introduced between the caudal two mammary glands (midline in bitches and cats, and just lateral to the penis in male dogs).
- The needle should be directed into the bladder caudally at a 45-degree angle.
- Aspirate urine.
- Stop aspirating prior to removal of the needle.

8.10 Cystocentesis.

leading to inappropriate treatment or communication of an inaccurate prognosis to the owner. The azotaemia in these cases generally fully resolves with appropriate fluid therapy (although hypercalcaemia can cause intrinsic renal damage if it persists), as with all cases of pre-renal azotaemia.

It is common for patients with chronic kidney disease (CKD) to develop a pre-renal azotaemia due to dehydration if they do not drink enough to compensate for their polyuria or if they have a concurrent disease process such as gastroenteritis causing increased fluid loss. These patients also present with isosthenuric urine but have both a pre-renal and a renal component to their azotaemia, with the extent of the renal component only becoming apparent once their fluid deficit has been restored.

Figure 8.1 lists methods of identifying a pre-renal azotaemia that can easily be performed in general practice. Less commonly used methods (generally requiring an external laboratory) of differentiating pre-renal and renal azotaemia include assessment of:

- Fractional excretion of sodium (FE_{Na}), which is calculated using the following equation:

$$FE_{Na} = 100 \times \frac{Na_{urinary} \times creatinine_{plasma}}{Na_{plasma} \times creatinine_{urinary}}$$

  (<1% consistent with pre-renal azotaemia and >1% consistent with renal azotaemia)
- Urine creatinine:plasma creatinine ratio (>20:1 consistent with pre-renal azotemia and <10:1 consistent with renal azotaemia).

Once an azotaemia has been recognized as being pre-renal in origin, fluid therapy is generally indicated. Fluid therapy is not indicated, however, if the pre-renal azotaemia is due to primary cardiac disease causing low cardiac output; instead, drug therapy to increase cardiac output and thereby renal perfusion is indicated. If diuretic therapy is being administered to a patient with cardiac disease to treat pulmonary oedema, a temporary mild pre-renal azotaemia may be a byproduct of effective treatment, although this should be monitored closely as it is possible for the patient to develop intrinsic AKI in this situation. Other therapies that may be required in patients with a pre-renal azotaemia include pressor therapy in patients with distributive or anaphylactic shock (see Chapter 3), anti-dysrhythmic therapy (see Chapter 6), treatment for obstructive shock (e.g. pericardiocentesis or gastric decompression), adjustment of drug therapy (e.g. vasodilator or anaesthetic drugs) and treatment of any underlying disease process.

Intrinsic AKI

Damage to the renal parenchyma can occur due to four different processes (Figure 8.11). The majority of intrinsic AKI is caused by ischaemic/nephrotoxic tubular necrosis and infection; however, the most common aetiologies in dogs and cats treated for AKI with haemodialysis were obstructive and unknown, respectively (Eatroff *et al*., 2012). Retrospective studies have shown poor overall survival rates: 35% survival for feline AKI (Lee *et al*., 2012) and 44% for canine AKI (Lee, 2011). The inclusion of haemodialysis as part of the management of AKI demonstrated similar survival rates: 50–60% for cats (Langston *et al*., 1997; Eatroff *et al*., 2012) and 47–53% survival for dogs (Segev *et al*., 2008; Eatroff *et al*., 2012). Although IRIS AKI grading has not been applied to survival analysis, survival rates decrease as patients become more azotaemic, as stratified by IRIS CKD staging, RIFLE (Risk, Injury, Failure, Loss, End-stage) classification, or other criteria (Lee *et al*., 2011; Thoen and Kerl, 2011; Eatroff *et al*., 2012). Hospital-acquired AKI has been shown to have a higher survival rate of 79% (Thoen and Kerl 2011).

Diseases involving large renal vessels
• Renal artery thrombosis or vasculitis • Renal vein compression (extra-renal)
Diseases of the renal microvasculature and glomeruli
• Glomerulonephritis • Vasculitis • Hypertension • Hypercalcaemia • Disseminated intravascular coagulation • Hyperviscosity syndrome
Ischaemic and nephrotoxic acute tubular necrosis
• Ischaemia caused by prolonged renal hypoperfusion • Exogenous toxins (chemotherapy, radiocontrast agents, ethylene glycol, raisins) • Endogenous toxins (myoglobin, haemoglobin)
Other acute processes involving the tubulointerstitium
• Neoplastic infiltration • Infectious

8.11 Causes of acute intrinsic renal azotaemia.

Diagnostic approach to intrinsic AKI

Determining whether a patient has underlying CKD may be difficult during an 'acute-on-chronic' injury to the kidneys. Historical, physical and diagnostic results may help identify pre-existing renal disease (Figure 8.12). Dogs with chronic renal disease have often acclimated to a certain degree of uraemia and therefore will present with less severe clinical signs than a patient with AKI that has the same degree of azotaemia.

Historical questioning of the owner may provide information regarding exposure to nephrotoxins (Figure 8.13). Travel history is important, to determine if the patient may have been exposed to infectious organisms (e.g. *Leptospira*, *Leishmania*) that can cause renal injury. Recent events that may have been associated with hypotension (e.g. sedation, anaesthesia, vomiting, diarrhoea, trauma) are risk factors for AKI.

A complete physical examination should be performed, with particular attention given to determination of hydration and perfusion status, presence of renal pain, size and surface texture of the kidneys, the size of the urinary

Parameter	AKI	CKD
History of PU/PD	Usually none	Present
Body condition score	Normal	Typically decreased
Renal size	Normal to increased	Decreased size 'Big kidney/little kidney' (unilateral fibrosis with ipsilateral hypertrophy)
Serum potassium	Normal to elevated	Decreased to normal
Haematocrit	Haemoconcentrated Blood loss anaemia (if uraemic ulcers are present)	Non-regenerative anaemia

8.12 Differentiating acute kidney injury (AKI) and chronic kidney disease (CKD). PU/PD = polyuria/polydipsia.

Group	Types
ACE inhibitors[a]	All
Antibiotics	Aminoglycosides (dose-dependent), carbapenems, cephalosporins, penicillins, quinolones, sulphonamides, tetracyclines
Antifungals	Amphotericin B (sodium desoxycholate formulation is more toxic than newer lipid formulations)
Antivirals	Aciclovir, cidofovir, indivir
Chemotherapeutics	Cisplatin, carboplatin, doxorubicin, methotrexate, streptozotocin
Diagnostic contrast agents	Gadolinium, iohexol
Diuretics[a]	All
Endogenous toxins	Haemoglobin, myoglobin
Food/plant toxins	Currants, grapes, lily plants, raisins
Herbal supplements	*Akebia* sp., *Datura* sp., *Ephedra* sp., *Glycyrrhiza* sp., *Taxus celebica*, Uno degatta
Immunosuppressives	Ciclosporin, rapamycin, tacrolimus
Miscellaneous toxins	Allopurinol, aminocaproic acid, bisphosphonates, dopamine, human intravenous immunoglobulin, hydroxyethyl starch, penicillamine, streptokinase, vitamin D-containing compounds
Non-steroidal anti-inflammatory drugs[a]	All
Organic compounds	Ethylene glycol, herbicides, pesticides, solvents

8.13 Nephrotoxins. [a] At normal dosages, these drugs have little nephrotoxicity in well hydrated, euvolaemic patients with normal renal function. Risk of toxicity greatly increases in states of hypoperfusion, accidental overdose, and in patients with renal impairment. ACE = angiotensin-converting enzyme.

bladder, and the presence of ascites or peripheral oedema. Moderately and severely azotaemic animals are often mildly hypothermic (typically 36.7–37.8°C), therefore normothermia (particularly in oliguric or anuric patients) may be considered as potential fever (Ash, 1991). Uraemic patients often have xerostomia (which may persist even in hypervolaemia), thereby making mucous membrane moisture an inaccurate metric of hydration status. Dehydration and hypovolaemia are common in AKI due to renal or gastrointestinal fluid losses.

Initial diagnostics should include a complete blood count, chemistry profile with electrolytes, urinalysis, blood pressure and imaging of the kidneys using ultrasonography and radiography. A urine sample obtained via cystocentesis should be submitted for aerobic culture and susceptibility testing prior to the administration of antibiotics. *Leptospira* testing should be performed when appropriate; a combination of urine and/or blood polymerase chain reaction (PCR) and serology should be performed. Many dogs will have negative or 'normal' initial antibody titres, therefore, convalescent titres should be evaluated 2–4 weeks after initial presentation. Previous vaccination can produce positive titre results; therefore, a 4-fold increase in antibody titres documented on a convalescent sample is suggestive of active disease. PCR results can be false-negative if the test has been submitted after antibiotic therapy has been initiated.

Many patients present with some degree of hypovolaemia or dehydration, making the initial differentiation between pre-renal and intrinsic renal AKI difficult. Pre-renal azotaemia should resolve after restoration of renal perfusion. Persistence of clinical signs and biochemical abnormalities indicates intrinsic renal damage.

The blood chemistry panel typically shows increased plasma creatinine, urea and phosphorus concentrations. Creatinine is an insensitive marker of GFR in AKI because time is needed for creatinine to accumulate in the plasma, and levels typically peak 7–10 days after an initial ischaemic event. Hypercalcaemia may be present in animals with hypoadrenocorticism, vitamin D toxicity and neoplasia. Hypocalcaemia may be seen in patients with ethylene glycol toxicity and pancreatitis. Hyperglycaemia can also be seen in ethylene glycol toxicity. Hyperkalaemia may be seen in animals with hypoadrenocorticism (typically accompanied by hyponatraemia), as well as oliguric or anuric presentations of AKI. Some patients may have hyperkalaemia that is severe enough to cause cardiac disturbances or death, and therefore should be recognized and treated immediately (see Chapter 5).

A complete blood count will provide information regarding the presence of anaemia or inflammation, as well as a platelet count. Haemoconcentration may be present in dehydrated or hypovolaemic patients. If anaemia is present, a reticulocyte count should be performed to assess for regeneration; however, it may take 3–5 days after the initial acute onset of anaemia before reticulocytes are seen in the circulation. Therefore, a reticulocyte count should be repeated after sufficient time has passed to make sure that the patient was not in a pre-regenerative state. Note that with severe AKI, renal production of erythropoietin may be decreased, and most patients have non-regenerative anaemia. Leucocytosis or leucopenia may indicate infectious or inflammatory disease; pyelonephritis should be considered a likely differential in this scenario. Thrombocytopenia can be seen with some glomerulonephropathies and infectious diseases such as leptospirosis. AKI is not commonly appreciated in rickettsial infections.

Urine volume is not helpful for initially differentiating the cause of azotaemia, due to the varying degree of pre-renal hypoperfusion that may be initially present. In animals with intrinsic AKI, urinalysis reveals isosthenuric (urine specific gravity 1.008–1.015) urine. Casts may be present on microscopic examination and are typically classified as cellular, granular or waxy. Cellular casts are further classified based on the cell type they contain. White blood cell casts are seen in animals with acute tubular necrosis, glomerulonephritis, pyelonephritis or nephrotic syndrome. Red blood cell casts are suggestive of vasculitis or glomerulonephritis. Epithelial casts represent tubular damage that is typically seen in acute tubular necrosis or an acute exudative glomerulonephritis. Granular casts are cellular casts that have undergone degradation. Glucosuria without hyperglycaemia represents proximal tubular dysfunction. This is not specific to any specific aetiology of AKI; however, pre-existing conditions such as Fanconi syndrome can produce the same urinalysis abnormalities (however, these do not typically cause AKI).

Abdominal radiography and ultrasonography should be obtained to evaluate renal size and architecture, and evidence of pyelonephritis, ureteral obstruction, ascites or bladder wall lesions. Particular attention should be paid to investigation for ureteral obstruction in cats (see below). Perirenal effusion has been associated with AKI; however, it is not specific to any aetiology. Intravenous pyelography with contrast agents should ideally be avoided in patients with AKI to avoid risks of contrast nephropathy; however, such studies may be necessary to diagnose ureteral obstruction and a balanced decision on the relative risk:benefit must be made for each individual patient. An

obstructed kidney will have decreased (or absent) GFR, thus resulting in diminished contrast uptake, making the interpretation of an intravenous pyelogram difficult. Anterograde pyelography may carry a smaller risk of contrast nephropathy and avoids the problem of diminished contrast uptake by the affected kidney. However, anterograde pyelography requires deep sedation, if not anaesthesia, and carries risks of urine leakage and haemorrhage.

Treatment of intrinsic AKI

The first step in the treatment of intrinsic AKI is to withdraw any nephrotoxic drugs. Similarly, drugs with potential nephrotoxicity should be avoided at all costs in patients with AKI. Intravenous fluids have long been revered as the cornerstone of AKI treatment. Patients should be assessed for hypoperfusion and this should be corrected according to its underlying cause (see above in treatment of pre-renal AKI). Only after hypovolaemia and dehydration have been corrected is measurement of urine output useful as an estimate of renal function.

The goal of intravenous fluid therapy is to restore renal perfusion. In polyuric patients this may require hourly fluid rates of three or more times normal maintenance requirements, depending on the intravascular volume deficit and ongoing losses through urine output. Close monitoring of cardiovascular and respiratory parameters, bodyweight, presence of oedema and urine output should be performed. In oliguric and anuric patients, measurement of central venous pressure may be helpful in recognizing hypervolaemia, as well as monitoring response to intravenous fluid challenge. Contrary to common dogma, fluid therapy does not increase renal function. Fluid rates of 10 ml/kg/h of an isotonic crystalloid resulted in no change in GFR in healthy anaesthetized dogs (Boscan *et al*., 2010).

The kidney is an encapsulated organ and can be severely adversely affected by fluid congestion and increased venous pressures, which can result in decreased renal blood flow and GFR. Thus, fluid overload must be prevented. Urinary catheterization with a closed collection system is critical in initial monitoring of fluid status (see Figures 8.3 and 8.6 to 8.8). Frequent comparison of the volume of intravenous fluid administered with urine output 'ins and outs' is crucial to monitor for oliguria or anuria and for prevention of fluid overload. Blood pressure and bodyweight should be recorded several times daily and trends monitored for hypovolaemia or hypervolaemia. Clinical signs of fluid overload include swollen conjunctiva (chemosis), serous ocular and nasal discharge, subcutaneous oedema (often particularly evident around the hocks in dogs), pulmonary oedema and ascites.

The initial fluid choice should be an isotonic crystalloid. Normal strength (0.9%) saline should be used in hypercalcaemic patients, as it may result in enhanced calciuresis. Shock doses of crystalloids should be administered for rapid correction of hypovolaemia, hypotension and hypoperfusion (see Chapter 4). Correction of dehydration should be performed over the first 12–24 hours. After fluid deficits have been replaced, in order to maintain normonatraemia, the administered fluid should be transitioned to a maintenance fluid with a lower sodium chloride concentration such as 0.45% NaCl, although fluids with very low or absent sodium, such as 0.18% NaCl and 4–5% dextrose, should be avoided. Potassium supplementation in intravenous fluids should be avoided or used cautiously in oliguric or anuric patients, as decreased urine output typically results in decreased potassium excretion, putting these patients at high risk of developing hyperkalaemia. Conversely, polyuric AKI often results in significant hypokalaemia, requiring significant potassium supplementation. Synthetic colloids should be used cautiously, as they have been shown to be an independent risk factor for developing AKI in humans (Mutter *et al*., 2013).

Patients should be given intravenous antibiotic therapy while urine culture results are pending. Initial empirical choice of antibiotic may be made based on suspicion of the underlying organism (Gram stain of a urine sample), or should be broad-spectrum. Once culture results are received, antibiotic therapy should be refined; alternatively, if urine culture is negative but pyelonephritis is still strongly suspected, broad-spectrum coverage should be continued. *Leptospira* are typically sensitive to penicillin and tetracycline-class antibiotics, as well as azithromycin. Note that many antibiotics have decreased excretion during states of renal impairment, thus requiring adjustment of dosage, frequency, or both. Tables of dosing guidelines are available in human medical textbooks and should be evaluated prior to administration. While drug pharmacokinetics may be different in feline and canine patients compared with humans, particular attention should be paid to drug dosing, particularly with drugs that have a small window of safety (e.g. fluoroquinolones in cats).

Blood pressure should be monitored and hypotension or hypertension should be treated appropriately (see Chapter 6). Hypertension can lead to renal sclerosis and failure to recover renal function. The development of hypertension throughout hospitalization is quite common, despite initial patient normotension, and is often suggestive of hypervolaemia (Geigy *et al*., 2011).

Nutrition is integral to supportive care and should be started early during hospitalization. Enteral feeding is preferable to ensure the health of enterocytes and to avoid the morbidity associated with parenteral nutrition. However, in nauseated patients with protracted vomiting, short-term parenteral nutrition should be initiated until enteral feeding is possible. Additional supportive care including antiemetics (e.g. maropitant, ondansetron, metoclopramide) and antacids is recommended. Decreased renal clearance of gastrin may promote the development of gastric ulceration and appropriate therapy should be instituted when necessary. Histamine-2 receptor antagonists require dosage adjustment in patients with renal impairment, whereas proton pump inhibitors (omeprazole, pantoprazole, esomeprazole) do not. This, along with their superior effect in gastric acid neutralization, suggests proton pump inhibitors to be the more favourable therapeutic option in patients with AKI. Nausea is common in uraemic patients, therefore antiemetic medications should be used to help provide patient comfort and prevent vomiting. Gastrointestinal ileus is often present, particularly in hypervolaemic patients. Prokinetic medications, such as metoclopramide, should also be considered.

Patient comfort and pain scoring should be performed and adequate analgesia should be achieved. Urinary obstructive disease, hypervolaemia, gastrointestinal ileus and ulceration are all painful conditions commonly occurring with uraemia. Opioid analgesics are a good initial choice; however, therapy should be individualized to the patient.

Anuria, oliguria and polyuria

Thorough monitoring should be performed to try to prevent a hypervolaemic state while ensuring maintenance of sufficient intravascular volume to optimize renal perfusion. Intravenous fluid therapy as well as water within enteral nutrition can precipitate hypervolaemia in oligoanuric patients, and polyuric patients are often less complicated

to manage while hospitalized. Most clinicians will try to convert an oligoanuric patient to a polyuric state. However, there is no evidence to suggest that increased urine output secondary to pharmacological intervention increases renal function in terms of GFR. Oligoanuria and failure to convert to polyuria may however represent a more severe renal injury; retrospective veterinary studies often show a higher mortality in these patients compared with polyuric patients. The pharmacological attempt to convert to polyuria should not delay a referral for renal replacement therapy.

Renin–angiotensin–aldosterone system activation in response to a volume-depleted state should result in decreased urine production. Therefore, urine output should be determined after hypovolaemia and dehydration have been corrected. Numerous definitions of oligoanuria have been proposed in the veterinary and human literature. The majority of renal injuries will result in a polyuric state; urine production <2 ml/kg/h should be considered oliguria. Urine production <0.25 ml/kg/h can be considered anuria.

Mannitol is an osmotic diuretic that results in transcellular shift of water, causing extracellular volume expansion. If it enters the glomerular filtrate, mannitol may increase tubular flow, which may maintain polyuria and help relieve intratubular obstruction from casts and debris. Theoretically, it can improve GFR and inhibit sodium reabsorption in the kidney by inhibiting renin release. The transcellular shift of water may result in hyponatraemia (via dilution of plasma) as well as hyperkalaemia (via solute drag), therefore mannitol should be used cautiously in patients with these pre-existing electrolyte disturbances. Mannitol is initially administered as a slow intravenous bolus of 0.25–1.0 g/kg. If urine production increases, mannitol may be administered as a constant rate infusion (CRI) of 1–2 mg/kg/min i.v. or 0.25–0.5 mg/kg i.v. q4–6h intermittent bolus therapy. Contraindications to mannitol therapy include intracellular dehydration as well as hypervolaemia. Human consensus guidelines suggest that mannitol should be avoided in humans with anuric AKI because of the risk of volume overload and hyperoncotic kidney injury if there is no urine output (Kellum *et al*., 2008).

Loop diuretics are commonly used to increase urine output and minimise damage to the renal tubular cells. By inhibiting the Na-K-2Cl transporter on the luminal surface of the thick ascending loop of Henle, these drugs have been thought to decrease oxygen consumption and lessen ischaemic damage. Additionally, by increasing urine flow, they may also reduce tubular obstruction. In order to be effective, these diuretics need to reach the tubular filtrate, which may not occur during anuric states. Controlled human studies have shown that furosemide was ineffective or even harmful when given to prevent AKI, can increase the risk of AKI when given to prevent contrast nephropathy, and is associated with an increased risk of death and non-recovery of renal function in established AKI (Mehta *et al*., 2008). The causality between furosemide administration and the development of AKI is yet to be determined; however, renal vasoconstriction due to reduced preload and decreased renal medullary perfusion has been observed (Levi *et al*., 2012). Despite these potential drawbacks, furosemide is still used in veterinary patients because it has been shown to convert some oliguric patients to polyuria, which facilitates management, especially if renal replacement therapy (RRT) is not available. An initial dose of 2 mg/kg i.v. of furosemide may be attempted, and bolus dose ranges of 2–6 mg/kg have been suggested. Increased urine output should be evident within 1 hour after administration. If effective, repeated bolus administration every 6–8 hours or a CRI of 0.25–1 mg/kg/h can be initiated.

Dopamine (0.5–3 μg/kg/min) has been advocated for the management of oliguric AKI via renal vasodilation, although it has not been proven to be effective in human studies. In addition, even at low doses, dopamine is potentially toxic in critically ill patients and can induce tachyarrhythmias and myocardial ischaemia. Based on these data, dopamine is not currently recommended for treating AKI in humans. Use of dopamine should be avoided in veterinary AKI due to a lack of documented benefit and the risk of adverse complications.

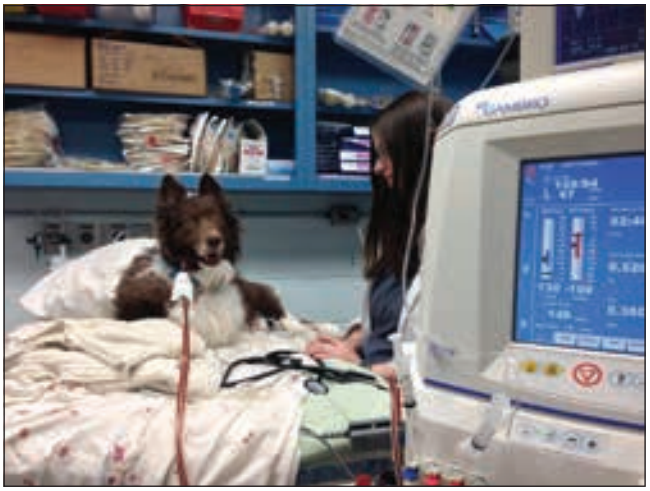
Fenoldopam is a selective postsynaptic dopamine receptor (D1) agonist that causes more potent renal vasodilation and natriuresis than dopamine. A placebo controlled study demonstrated fenoldopam increases FE_{Na} and GFR in healthy dogs (Kelly *et al*., 2016). However, it can also promote hypotension by decreasing systemic vascular resistance. A study in healthy cats showed that an average 4-fold increase in urine output occurred approximately 20 hours after fenoldopam (0.5 mg/kg/min for 2 hours i.v.) administration (Simmons *et al*., 2006). Only one retrospective study has been published evaluating fenoldopam in azotaemic animals; its usage was not associated with improved survival in animals with AKI (Neilsen *et al*., 2015).

Renal replacement therapy

Indications for RRT include symptomatic uraemia, acidosis, hyperkalaemia, or volume overload that is refractory to medical management (Figure 8.14). Referral for these conditions should occur early, as a delay in extracorporeal therapy results in higher morbidity and mortality in human studies. RRT includes peritoneal dialysis (PD) and extracorporeal therapy such as intermittent haemodialysis (IHD) (Figure 8.15) and continuous renal replacement therapy (CRRT).

- Inadequate urine production
- Life-threatening pulmonary oedema or fluid overload
- Hyperkalaemia or other life-threatening electrolyte or acid–base disturbance
- Progressive/refractory azotaemia
- Diuretic-resistant congestive heart failure or severe overhydration in the absence of renal disease
- Acute poisoning/drug overdose with a substance that can be removed by dialysis

8.14 Indications for renal replacement therapy.



8.15 A dog undergoing intermittent haemodialysis.

Peritoneal dialysis has historically been performed more commonly in veterinary medicine due to its relative 'low tech' requirements and the sparse availability of haemodialysis. This is changing with the development of worldwide RRT centres (see www.asvnu.org for a current list of veterinary hospitals). Referral for RRT is recommended wherever possible but, if unavailable, PD is still worth considering. PD temporarily replaces renal excretory function by using the peritoneum as the semipermeable membrane across which unwanted solutes are eliminated. This is performed by inserting a multilumen catheter into the peritoneum and instilling a dialysate fluid. Dialysate is infused into the abdomen, and time is allowed for redistribution of solutes into the dialysate fluid before removal, and a new cycle is begun. This process is described in excellent detail elsewhere (Bersenas, 2011). PD is contraindicated in patients with intra-abdominal conditions that prevent safe dialysate exchange, such as abdominal wall trauma and peritoneal infections or adhesions that lead to loss of more than 50% of the peritoneal surface. PD is also contraindicated in severe catabolic states in which marked hypoalbuminaemia exists, because large amounts of protein can be lost through the peritoneum during dialysis. The most frequent complications are the development of peritonitis (reported in 22% of veterinary patients), catheter occlusion, excessive protein loss, pleural effusion and dialysis disequilibrium syndrome.

Dialysis disequilibrium syndrome is a neurological complication that has been reported in both PD and IHD patients. The exact cause is unknown; however, the prevailing theory suggests that rapid removal of urea from the intravascular space results in an expected parallel decrease in serum osmolality, though the removal of urea and other uraemic toxins from the central nervous system is slower. Thus, the brain parenchyma will have a higher osmolality than the serum, resulting in cerebral oedema. Clinical signs of dialysis disequilibrium may be seen during or up to 48 hours after a dialysis session, and may include agitation, altered mentation, seizures and even death due to cerebral herniation. CRRT is thought to have an inherent decreased risk of causing dialysis disequilibrium due to the slow removal of uraemic toxins from the intravascular space.

Extracorporeal therapies require specific training for successful patient management. IHD and CRRT differ in their rate of solute removal, duration of therapy, intensity of treatment, cost and required equipment. Excellent reviews have recently been published regarding extracorporeal blood purification in veterinary medicine (Aceirno, 2011; Bloom and Labato, 2011). In human medicine, studies have shown no significant difference in mortality and morbidity when comparing patients treated with IHD or CRRT. Both therapies perform blood purification via diffusion and/or convection across a dialyser (artificial kidney). Patients must receive anticoagulant therapy to prevent coagulation in the disposable blood tubing or dialyser. Anticoagulation is most commonly performed using unfractionated heparin as a CRI during a dialysis session. Regional anticoagulation using citrate and calcium gluconate can be performed to produce blood that is anticoagulated while within the extracorporeal circuit, and preventing systemic anticoagulation of the patient. This technique is most commonly used in hypocoagulable patients already at risk of haemorrhage or coagulation complications.

The dialysis prescription must be made for each individual patient, accounting for uraemia, volume status, electrolyte disturbances and acid–base status. Survival rates of veterinary dialysis average around 40–60%; however, the prognosis varies depending upon the underlying aetiology. Infectious and obstructive causes typically have the best prognosis, whereas toxic aetiologies carry less favourable outcomes. The reported survival rate of patients treated with renal replacement therapy is particularly notable, as nearly all of these animals had already failed medical management. Numerous toxins, notably ethylene glycol and the toxic component of lily plants, can be removed via renal replacement therapy, thus preventing prolonged exposure and helping to prevent systemic toxicity (Monaghan and Acierno, 2011). Haemoperfusion can also be performed to remove some toxins that are more extensively protein bound, such as some NSAIDs. This process involves the addition of a charcoal filter to the extracorporeal circuit, through which blood passes. The charcoal non-specifically adsorbs toxins and facilitates their removal.

Post-renal azotaemia

A post-renal azotaemia can occur secondary to dysfunction of the ureter(s), bladder or urethra. Inability to void urine results in the same metabolic and electrolyte disturbances as intrinsic renal dysfunction, but often treatment of the underlying pathology is easier and more effective.

Ureteric obstruction

Obstruction of a single ureter does not lead to azotaemia unless there is concurrent pathology in another part of the renal or urinary system, as a decrease in GFR of greater than 75% is required before azotaemia develops. However, this is not uncommon, as ureteral obstruction most frequently occurs due to ureterolithiasis in cats and dogs, and if a cat or dog is prone to urolith formation then repeated or bilateral obstruction episodes can occur. Studies suggest that permanent renal damage results after ureteral obstruction for 7 days in dogs (Berent, 2011) and so CKD can develop. Cats therefore often present with one enlarged kidney (with ureteric obstruction and hydronephrosis) and one small kidney (with CKD) noted on physical examination. Dogs more commonly present with renal pain noted on physical examination.

Ureteric obstruction is confirmed with diagnostic imaging. Radiography can reveal radiopaque ureteroliths (the vast majority of ureteroliths in cats, and approximately 50% in dogs, are reported to be radiopaque calcium oxalate) (Figure 8.16). Performing a warm water enema (phosphate enemas are contraindicated in the azotaemic patient) may be beneficial to aid visualization of ureteroliths, as the colon overlies the ureteral path on radiographs.



8.16 Lateral abdominal radiograph demonstrating many ureteral calculi in a cat. Note the decreased size of the left kidney and the presence of renoliths suggestive of chronic kidney disease.

Abdominal ultrasonography can sometimes demonstrate ureteroliths, but more commonly hydronephrosis and ureteral dilatation proximal to the obstruction are visualized, although this may take several days to develop. The combination of abdominal radiography and ultrasonography has been demonstrated to have the highest sensitivity in finding feline ureteroliths (Kyles *et al*., 2005).

Treatment of ureteroliths is not straightforward. A conservative approach with fluid therapy to attempt to 'flush' the stone can be used and should be initiated once the diagnosis has been made even if more invasive therapy is planned. Drug therapy (including mannitol, furosemide, alpha-adrenergic antagonists, amitriptyline and glucagon) is sometimes used in conjunction with fluid therapy. One study reported that fluid therapy in conjunction with diuretics resulted in resolution of the ureteral obstruction in fewer than 10% of cats (Kyles *et al*., 2005). If medical management fails to result in passage of the ureterolith within 48–72 hours or if the patient is deteriorating or clinically unstable, then interventional therapy is recommended. Various options are available:

- **Ureterotomy:** Sometimes in conjunction with ureteral re-implantation into the bladder, this has been the traditional surgical method used for ureteroliths. This is technically a very demanding surgery requiring an operating microscope and experienced surgeons. Complications include ureteral oedema, re-obstruction and uroabdomen due to leakage from the surgical site
- **Ureteral stent placement:** This involves placing a stent either in a retrograde fashion via a cystotomy (or cystoscopy in dogs) or anterograde via the renal pelvis into the obstructed ureter. In some circumstances the stent is placed via a ureterotomy in cats. The ends of the stent sit in the renal pelvis and the bladder and the stent bypasses the obstruction. The stents are designed for temporary use in humans but are not removed in cats and dogs unless a complication occurs. The most common complication is dysuria
- **Subcutaneous ureteral bypass:** This technique involves connecting the renal pelvis to the bladder via a nephrostomy tube and a cystotomy tube, both tunnelled subcutaneously and connected via a special port. This is a quicker and simpler technique than stent placement and is thought to be associated with fewer complications (Berent, 2011)
- **Nephrostomy tube placement:** This can provide temporary management of a patient with a suitably enlarged renal pelvis (>10 mm) prior to referral for definitive treatment. They can also be used as a treatment strategy as the decrease in renal pelvic and ureteral pressures may relieve ureteral spasm and oedema, leading to ureterolith movement. The risk of tube dislodgement is significant and so complication rates are higher than with other management methods (Kyles *et al*., 2005)
- **Lithotripsy:** Either extracorporeal or via ureteroscopy, can be used to administer shockwaves to a ureterolith and fragment it. However, in cats without ureteral dilatation, the fragments produced are still too large to pass down the ureter and so this therapy is often unsuccessful.

Ureteroscopy can be performed in some large dogs with ureteral dilatation and this allows direct lithotripsy of ureteroliths or ballooning of strictures.

Although ureteroliths are the most common cause of ureteral obstruction, other possibilities include iatrogenic obstruction (most commonly following ovariohysterectomy), idiopathic strictures, blood clots and neoplasia. The treatment options described above can also be used for these disease processes.

Rupture of the urinary tract

Trauma can lead to damage to any part of the urinary system, from the kidney to the urethra, resulting in urine leakage. Urinary tract damage and leakage can also occur iatrogenically, most commonly secondary to urethral catheterization, overzealous manual expression (often in combination with urethral obstruction) or surgery of the urinary tract. Regardless of the underlying cause, uroretroperitoneum (due to leakage from the kidney(s) or proximal ureter(s) with an intact peritoneum), uroabdomen (due to leakage from the distal ureter(s), bladder or proximal urethra) and/or urine accumulation in the area of the caudal ventral abdomen and hindlimbs (due to urethral damage) can all result. The most commonly traumatized locations are the bladder and urethra. It is important to note that a palpable bladder and the ability to void a stream of urine without gross evidence of haematuria does not preclude bladder or urethral trauma or indeed urinary tract rupture at any point.

Urinary tract rupture should be suspected in any animal with azotaemia and hyperkalaemia after trauma, particularly if the patient was previously healthy. Pelvic fractures and/or haematuria in the post-trauma patient or a history of a traumatic urethral catheterization should also prompt the clinician to consider the possibility of a rupture. Free abdominal fluid can be rapidly identified ultrasonographically, although blind abdominocentesis should be performed if ultrasonography is not available and uroabdomen is suspected (see Chapter 11).

Once abdominal fluid is obtained the levels of creatinine, potassium and urea can be checked and compared with plasma levels. In dogs, a ratio of creatinine in abdominal fluid to that in plasma of ≥2:1 and a ratio of potassium in abdominal fluid to that in plasma of ≥1.4:1 have been shown to be strongly suggestive of uroabdomen (Schmiedt *et al*., 2001). Cytological examination of the fluid should also be performed immediately, as the fluid may be septic if concurrent gastrointestinal tract injury is present, or if a urinary tract infection was previously present.

Once the patient has been stabilized (see 'Emergency management of the AKI patient' above) a contrast study can be performed to identify the location of the rupture. Given that urethral or bladder rupture are the most likely causes of uroabdomen, a retrograde urethrocystogram is the most appropriate study. If there is no evidence of leakage then an intravenous urogram can be performed, but care should be taken that the patient is adequately stabilized and that suspicion for renal or ureteral trauma is very high, as radiopaque contrast agents are nephrotoxic and could initiate or worsen AKI.

Management of urinary tract rupture depends on the site of damage. Initial stabilization is the same for all patients, however. Fluid therapy is required to correct any hypovolaemia or dehydration. Placement of a urethral catheter (see Figures 8.3 and 8.6 to 8.8) if possible allows urine drainage in patients with urethral or bladder rupture, either by bypassing the leak or by preventing bladder filling and therefore leakage. Many urethral ruptures are partial and therefore catheterization is often possible and should be attempted. If a uroabdomen is present then drainage of the abdominal fluid can aid correction of hyperkalaemia (and azotaemia, although this is of lesser importance).

Drainage of a uroabdomen (with or without placement of a peritoneal drain) can often be performed in a conscious patient as the procedure is not unduly painful or distressing and the patient is usually quiet due to their underlying disease process (see Chapter 11 for details of therapeutic abdominocentesis).

If renal damage causing urine leakage is present then a ureteronephrectomy is generally required. Ureteral rupture may be treated by ureteral reimplantation into the bladder if the damage is sufficiently distal, but again ureteronephrectomy is often required. Bladder rupture usually requires surgical repair, although very minor rents, e.g. due to a complication of cystocentesis, can be managed with urethral catheter placement and continuous bladder drainage for several days. Urethral tears can occur secondary to trauma (often seen in conjunction with pelvic fractures) or iatrogenically after attempted urethral catheterization. Surgical repair may be required but urethral tears can often be managed conservatively via the maintenance of a urethral catheter. If unable to place a urethral catheter in a retrograde fashion, fluoroscopy can be used to assist in passing a guide wire from the bladder through the urethra in an anterograde fashion, allowing the wire to now serve as a guide for retrograde placement of the urethral catheter (see Figures 8.3 and 8.6 to 8.8). There is a risk of urethral stricture with either surgical or conservative management of urethral tears.

In patients with complicated urethral or bladder rupture, tube cystotomy may be useful to allow temporary urinary diversion. This can allow stabilization of the patient prior to referral or provide time for inflammation to decrease prior to definitive surgical therapy. Cystotomy tube placement is fairly straightforward using a mushroom-tipped catheter placed into the ventral aspect of the bladder through a stab incision made in the centre of a purse-string suture, which is then tightened to secure the catheter. The catheter should exit the body wall through a paramedian incision.

Urethral obstruction

Urethral obstruction is a common emergency presentation in male cats but is very rare in queens. Feline lower urinary tract disease (FLUTD) is a term used to cover a wide range of disorders affecting the bladder or urethra of cats, including urolithiasis, bacterial infections, neoplasia, urethral plugs and idiopathic disease. Despite the variation in underlying causes, the resulting clinical signs are similar and include dysuria, stranguria, haematuria (macroscopic and microscopic), pollakiuria and periuria (Hostutler *et al*., 2005). Cats affected with FLUTD can develop urethral obstruction, with the most frequent cause of obstruction being a urethral plug (made up of protein, erythrocytes, leucocytes and crystals) or idiopathic cystitis. Urolithiasis, neoplasia and strictures can also cause obstruction.

Although not seen as frequently as in male cats, urethral obstruction is not uncommon in male dogs. Obstruction in the bitch occurs very rarely. Obstruction is generally secondary to urolithiasis in dogs with a strong genetic predisposition to urolith formation, for example urate urolithiasis in Dalmatians due to decreased hepatic transport of urate preventing an adequate rate of conversion to allantoin. Dogs with congenital portosystemic shunts are also predisposed to urate urolithiasis.

Both dogs and cats affected with urethral obstruction often have a history of straining to pass urine (although this can be mistaken for straining to pass faeces in cats and may not even be noticed by the owners of cats that do not use a litter tray). On physical examination a large, tense bladder is easily palpable in cats and often noted in dogs. Presentation varies from complete stability to cardiovascular collapse due to hyperkalaemia and acidosis. It is rare for dogs to develop clinically significant hyperkalaemia.

All patients with urethral obstruction require a full and thorough physical examination, initially focusing on the major body systems as life-threatening hyperkalaemia may be present (see Chapter 5 for management). The patient should be stabilized while preparation for sedation and urethral catheterization is made. An intravenous catheter is placed and bolus intravenous fluid therapy with either 0.9% NaCl or Hartmann's solution is appropriate (as described in Chapter 4). Performing cystocentesis (see Figure 8.10) in these patients is contentious, as there is a risk of causing rupture of a compromised bladder or a uroabdomen through leakage from the cystocentesis site. Cystocentesis is generally not necessary unless urethral catheterization fails.

The majority of cats require sedation to allow urethral catheterization (see Figures 8.3 and 8.6) but in those that are severely collapsed this may not be necessary. In these patients, urethral catheterization should be performed as rapidly as possible concurrent with attempts to stabilize the patient's cardiovascular system through fluid and drug therapy (see Chapter 5 for emergency management of hyperkalaemia). In most cats, however, adequate sedation is important to allow passage of the urinary catheter, both to prevent patient movement and also to increase urethral relaxation. A sedation protocol of 0.25 mg/kg midazolam with 2.5 mg/kg ketamine i.v. is often effective, but if the cat is not fully sedated a further 2.5 mg/kg ketamine can be administered. If the obstruction is marked then general anaesthesia may be appropriate to give more time for catheterization to be performed. Sedation (e.g. 0.3 mg/kg butorphanol i.v. with or without 0.02 mg/kg acepromazine in a stabilized dog) or more commonly full general anaesthesia is generally required for urethral catheterization of the obstructed dog (see Figures 8.7 and 8.8). If urethral catheterization is not possible, an alternative to repeated cystocenteses is placement of a cystotomy tube as described above.

Once a urethral catheter has been placed, the patient should be monitored closely during recovery from sedation or anaesthesia. Those that were cardiovascularly collapsed prior to urethral catheterization often have a prolonged recovery. If insulin was used to control hyperkalaemia its action can be surprisingly prolonged in these patients (even if neutral insulin was used) and so monitoring for hypoglycaemia is important. A post-obstruction diuresis is common and so urine output should be closely monitored. Initially, monitoring urine output every hour is advisable and fluid therapy should be titrated so that dehydration and/or hypovolaemia does not develop – i.e. 'ins' should match 'outs'.

The diuresis leads to hypokalaemia in most cases so monitoring serum potassium is important, with supplementation required in the isotonic fluids. Patients should be kept comfortable with analgesia; until the patient is fully stable, opioid analgesia such as buprenorphine is appropriate. NSAIDs can be used once the patient is no longer azotaemic and is eating and drinking normally.

Antibiotics are not routinely required by patients with urethral obstruction unless bacteria or severe pyuria are seen on urine sediment examination (it is worth noting that urine dipsticks designed for humans are inaccurate for assessing the presence of white blood cells in feline urine). If bacterial infection is suspected, urine should be cultured

to allow appropriate antibiosis to be used and a broad-spectrum antibiotic such as potentiated amoxicillin used whilst awaiting results. Although urinary catheter bacterial colonization is common, this generally does not lead to an ongoing bacterial urinary infection once the catheter is removed. Therefore, urine culture, if performed, should be submitted at least 48 hours post catheter removal. Urine culture is generally indicated only if the patient is showing clinical signs consistent with a urinary tract infection. However, any urolith or plug obtained during catheterization should be cultured and analysed for chemical make-up to allow appropriate therapy. The presence of crystals in feline urine on sediment examination is of little diagnostic significance, however, and their presence should not be interpreted as the definitive cause of obstruction.

Urolith analysis is extremely important in dogs, as urolithiasis is the most common cause of urethral obstruction, and dietary management is often required to prevent recurrence of the disease. Cystotomy or lithotripsy (if the patient and the cystoliths are of an appropriate size) is required after de-obstruction in dogs and some cats, although this can be delayed once a urinary catheter has been placed. Surgery can then be performed once the owners and clinicians are ready or referral to an institution that performs lithotripsy can be arranged.

Repeat urethral obstruction is a common problem in cats and there is debate over the optimum length of time for urinary catheterization. It is likely that it is patient-dependent and that the catheter should remain *in situ* at least until the urine being produced is no longer sanguineous. Recurrence of obstruction is reported to occur in 20–60% of cats. Once the urinary catheter has been removed the patient should be monitored closely for signs of re-obstruction, although whether this should be done in the hospital is debatable given the role of stress in the FLUTD syndrome. Cats with idiopathic cystitis have been shown to have an imbalance between the sympathetic nervous system and cortisol production (Dru Forrester and Roudebush, 2007) and therefore decreasing stress is thought to be an important component of management of these cases. If the patient is discharged prior to demonstrating adequate urination, the owner must be made aware of the importance of monitoring the patient closely and the risk of re-obstruction. Muscle relaxant drugs such as phenoxybenzamine (0.5–1 mg/kg orally q12h), prazosin (0.25–1 mg/cat orally q8–12h) and dantrolene (0.5–2 mg/kg orally q12h) have all been shown to decrease feline urethral pressure experimentally. A retrospective study found an association between prazosin use and decreased rate of re-obstruction compared with the use of phenoxybenzamine in clinical patients (Hetrick and Davidow, 2013). Factors associated with an increased risk of feline urethral obstruction include obesity, being fed a dry food and being an indoor cat, so changing these factors if possible may reduce the risk of recurrence.

Non-obstructive lower urinary tract disease

In patients presenting with dysuria, stranguria, pollakiuria, haematuria and/or periuria the priority is to confirm whether urethral obstruction is present; this is generally obvious through the identification of a large, tense bladder on physical examination. If it is not then other differentials need to be considered, including feline idiopathic cystitis, bacterial cystitis, neoplasia, prostatic disease, perineal hernia and urolithiasis. After obtaining a full history and performing a thorough physical examination, assessment of a urine sample obtained via cystocentesis (see Figure 8.10) is generally required. Urinalysis with cytological examination and dipstick and assessment of urine specific gravity, with or without urine culture, will aid narrowing of differentials and the choice of either appropriate symptomatic treatment or further diagnostics. In feline patients with non-obstructive idiopathic cystitis, urinalysis can be unremarkable but haematuria and pyuria are fairly common findings (Defauw *et al*., 2011). These cases are often therefore suspected to be bacterial cystitis and treated unnecessarily with antibiotics. If bacteria are not seen on cytological examination of a cystocentesis urine sample then it is recommended that culture is performed prior to initiation of antibiotic therapy. Bacterial cystitis is more common in dogs, and symptomatic therapy with broad-spectrum antibiotics such as potentiated amoxicillin may be appropriate if it is the patient's first presentation with suspected bacterial cystitis. If repeated episodes occur then investigation for an underlying cause and culture of a urine sample obtained via cystocentesis is recommended.

Retroflexed bladder in perineal hernia

Perineal hernias are generally seen in older male dogs, although they are also seen in bitches and cats. Bladder retroflexion is reported to occur in 20–25% of dogs with perineal hernias, resulting in stranguria. Although post-renal azotaemia is not uncommon in these patients, hyperkalaemia and cardiovascular instability are rare. Bladder retroflexion can be confirmed fairly easily with ultrasonography, but radiography can also be diagnostic if ultrasonography is not available, with the use of a positive or negative contrast cystogram if required. If the patient is unable to void urine then a urinary catheter should be placed with care. Due to the displacement of the bladder there is an increased risk of iatrogenic damage to the urethra and bladder. Once a catheter is *in situ* the bladder should be drained and the catheter kept in place until surgical repair of the hernia is performed. If a catheter cannot be passed then perineal cystocentesis can be performed to allow decompression of the bladder, which often results in the clinician being able to reposition the bladder with manual pressure on the perineal region. If this is successful, urinary catheterization should be performed. If the bladder cannot be replaced in the abdomen, the patient should undergo surgery and a cystopexy may be performed along with perineal hernia repair and castration of entire male dogs.

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Chapter 9

Neurological emergencies

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Diseases of the nervous system may manifest acutely and necessitate immediate intervention. Alternatively, they may develop over time; in this scenario it is still essential that they be identified and treated at an early stage to prevent a chain of events that could result in a self-propagating deterioration in the patient's condition. A review of the more common neurological emergencies in companion animals is presented below.

Performing an emergency neurological examination

Whenever possible, it is best to perform a full neurological examination early in the patient's evaluation. However, if time is of the essence, an abbreviated neurological examination can be performed that will give enough information to draw up a problem list, localize the lesion(s) and prioritize care.

Broadly speaking, the abbreviated emergency neurological examination involves evaluation of three components:

- Ambulation
- Mental status
- Cranial nerve function.

Ambulation

- Is the animal walking? If yes, is the animal walking normally or abnormally? If abnormally, is the animal ataxic? How many limbs are affected: pelvic limbs, all four, or one side of the body? Is there circling, or is the animal walking compulsively or head pressing?
- If the animal is not walking, is there evidence of voluntary motor function in the affected limbs?
- Is there involuntary motor function (i.e. seizure activity)?
- A brief postural ability test should be performed on each limb: ability to replace a knuckled-over paw and hopping are sufficient.
- Withdrawal reflexes should be assessed in all four limbs. While this is being performed, look for conscious recognition of stimulation (e.g. head turning, vocalizing) in addition to palpating the limb for muscle tone and evidence of muscle atrophy. Loss of conscious recognition of pain (known as deep pain) is a concerning sign (see section on Pelvic limb paresis and paralysis). It is important to note that an intact withdrawal response does not indicate an intact spinal cord pain pathway.

Before moving the animal for additional tests, be sure to evaluate the history for possible traumatic fracture/luxations (i.e. hit by car, falls) and take necessary precautions if suspected (see Head trauma section).

Mental status

- Assess the level of consciousness of the animal. Alert? Depressed? Sleepy but rousable by voice/touch? Unrousable?
- Look for response to a single clap of the hands. Does the animal sit up/turn around? Do the ears twitch? Is there no response?
- Look for response to touching around the face, especially the nasal planum, medial canthus of the eyes, and ears.
- If there is no response to either sound or touch, look for a response to noxious stimulus (e.g. pinch the nasal planum or lips with haemostats. As before, look for conscious recognition when performing withdrawal responses).

Cranial nerve function

In an emergency, testing of the following cranial nerves (CN) is often sufficient to localize the lesion and provide an indication of the severity of clinical signs at the same time. The cranial nerves that should be tested include:

- Menace response (CN II/visual pathway): is there a blink (CN VII) and/or retraction (CN VI) of the globe when the eye is menaced?
- Pupil size (CN III): look for symmetry and note size (small, medium, large)
- Pupillary light reflex (CN II/III): look for response to light (direct and consensual)
- Examine the oculovestibular reflex (CN III/IV/VI/VIII): look for normal physiological nystagmus when the head is moved horizontally and vertically. Also look for abnormal nystagmus when the head is at rest and positional nystagmus when the patient's position is altered (e.g. turned on its back)
- Assess for a gag reflex (CN IX/X/XII)
- The ocular fundus should also be examined for the presence of chorioretinitis or papilloedema.

Triaging the neurological patient

Following the neurological examination, it should be possible to localize the patient's lesion into one or more of the following categories (Figure 9.1):

- Intracranial:
  - Abnormal mental status
  - Seizure activity
  - Abnormal cranial nerve examination
  - Compulsive pacing/head pressing (if walking)
- Spinal. Normal mentation with:
  - C1–C6: proprioceptive deficits in all four limbs, normal or exaggerated withdrawal reflexes in all four limbs
  - C6–T2: proprioceptive deficits in all four limbs (usually worse in pelvic limbs), normal or exaggerated withdrawal reflexes in pelvic limbs but abnormal/reduced withdrawal reflexes in the forelimbs
  - T3–L3: proprioceptive deficits in pelvic limbs only, normal or exaggerated withdrawal reflexes in the pelvic limbs
  - L4–S3: proprioceptive deficits in the pelvic limbs, reduced or absent withdrawal reflexes in the pelvic limbs, possible urinary/faecal incontinence and reduced anal sphincter tone
- Peripheral nerve:
  - Proprioceptive deficits in one or more limbs with decreased withdrawal reflexes
  - Normal mentation
  - Hypoventilation possible
- Multifocal:
  - Neurological dysfunction indicating involvement of more than one region.

Further specific detail of the neurological examination findings and subdivision of the categories mentioned above can be found in Figure 9.1.

Prioritizing care

The results of the neurological examination help to identify which parts of the nervous system show evidence of malfunction. The next step is to determine what disease process is likely to be causing the neural dysfunction. This may not always be possible in the emergency room environment; therefore, the clinician should attempt to identify problems that can immediately endanger the life of the patient, which include loss of consciousness and coma, head trauma and seizures or status epilepticus. These will be addressed first in this chapter.

Vascular disease, while common in human patients, infrequently results in critical disease in veterinary patients. Metabolic encephalopathies, vestibular and cerebellar disorders, diseases causing paraparesis or tetraparesis, and diseases causing episodic weakness or abnormal neuromuscular function are unlikely to result in the sudden death of the patient. However, failure to identify these disorders and institute appropriate therapy promptly may result in deterioration of the patient with possible life-long consequences. For example, it is common for a client to discontinue further therapy once a dog with neuromuscular disease deteriorates to the point of developing aspiration pneumonia. It is also common for a client to elect to euthanase a dog that is paraplegic but otherwise normal. Spinal cord and neuromuscular disorders will be presented at the end of this chapter.

Loss of consciousness and coma

Stupor is a state of depressed consciousness in which the animal is responsive only to strong, often noxious stimuli. Coma is a state of unconsciousness in which the animal is not aroused even by noxious stimuli. Both may result from severe, bilateral and diffuse dysfunction of the cerebral hemispheres and/or destructive or compressive lesions of the brainstem involving the ascending reticular activating system.

Evaluation of the stuporous or comatose patient

The neurological examination should be used to localize the likely site of the pathology (cerebrum or brainstem) leading to the stupor/coma. Regardless of neurolocalization, gait and postural ability are non-existent in stuporous or comatose animals. Segmental reflexes are normal or hyperreflexive.

Cerebral hemispheres/diencephalon

Cranial nerves: Diffuse bilateral disease of the cerebral hemispheres and diencephalon may cause blindness and bilaterally miotic pupils that are responsive to light. No abnormalities of physiological nystagmus are found.

Other: Cheyne–Stokes respiratory pattern may occur (periods of tachypnoea interspersed with prolonged apnoea). Rhythmic walking movements may be elicited if the animal is supported.

Brainstem

Cranial nerves: Dependent on the precise location and extent of the abnormality, there is variable cranial nerve involvement. The animal may or may not respond to visual testing. Unilateral or bilateral fixed mid-position or dilated pupils, ipsilateral or bilateral ventrolateral strabismus, and abnormal or absent physiological nystagmus may occur. Absent physiological nystagmus may be a poor prognostic sign in animals with brainstem disease. Physiological nystagmus occurs as a result of vestibular centre projections via the medial longitudinal fasciculus (MLF) to the nuclei of CN III, IV and VI. The MLF runs deep within the brainstem, and as a result, lesions that are severe enough to disrupt the MLF indicate severe brainstem damage. However, depressed or absent oculovestibular movements have also been seen in some animals with severe metabolic disease, and have resolved following therapy of the underlying metabolic defect. Signs of CN V–XII dysfunction may occur.

Other: Apnoea or hyperventilation may occur. A decerebrate posture may be seen, manifested by extension of all four limbs and opisthotonos.

Causes and treatment of stupor or coma

Diffuse dysfunction of the cerebral hemispheres

Inflammatory diseases, lysosomal storage diseases, metabolic diseases, neoplasia with associated oedema, infection and hydrocephalus can cause signs of diffuse cerebral hemisphere/diencephalic dysfunction. Treatment is directed at the inciting cause and at decreasing intracranial pressure (ICP) (see Head trauma below).

Mental status	Gait	Postural ability	Segmental reflexes	Sensation	Cranial nerve function	Other
Cerebral hemispheres/diencephalon						
Depression, disorientation, stupor, coma; other abnormalities such as aggression and hyperexcitability	Circling (frequently toward the side of the lesion), pacing or head pressing. Otherwise gait is normal	Postural reaction deficits contralateral to the lesion	Normal	Depressed over the face and limbs contralateral to the lesion	Blindness contralateral to the lesion with normal pupillary responses. Bilateral miosis with responsive pupils with diffuse cerebrocortical disease. Dilated pupils, non-responsive to light (fixed) when disease involves the optic chiasm	Seizures. Abnormalities associated with hypothalamic involvement. Cheyne-Stokes respiration
Midbrain						
Depression, stupor or coma	Ataxia and spastic tetraparesis/paralysis. Contralateral spastic hemiparesis/paralysis and ataxia if the lesion is lateralized	Postural reaction deficits contralateral (common) or ipsilateral (less common) to the lesion. Increased extensor tone of the limbs contralateral to the lesion. Decerebrate posture, characterized by opisthotonus with rigid extension of all limbs	Hyperreflexia of the limb reflexes contralateral to the lesion	Depressed below the level of the lesion	A dilated and fixed pupil and ventrolateral strabismus ipsilateral to the lesion due to CN III involvement. Bilateral miosis due to CN III stimulation. Dorsolateral rotation of the globe (CN IV)	Hyperventilation
Pons/medulla						
Depression, stupor or coma	Ataxia and spastic tetraparesis/paralysis. Ipsilateral spastic hemiparesis/paralysis and ataxia if the lesion is lateralized	Postural reaction deficits and increased extensor tone of the limbs ipsilateral to the lesion, or of all four limbs if lesion involves both sides of the pons/medulla	Depressed ipsilaterally below the level of the lesion	Decreased over the side of the face ipsilateral to the lesion	Decreased sensation of the face, decreased jaw tone, masticatory muscle atrophy (CN V); decreased palpebral reflex (CN V and VII); medial strabismus, decreased globe retraction (CN VI); drooping lips, inability to blink the eyelids or move the ears (CN VII); nystagmus, head tilt and positional ventral strabismus (CN VIII); dysphagia, dysphonia, decreased gag reflex (CN IX and X); regurgitation, megaoesophagus (CN X); decreased tongue motion and tongue muscle atrophy (CN XII) ipsilateral to the lesion	Rapid, shallow breathing; irregular, ataxic breathing; or apnoea
Cerebellum						
Normal	Dysmetria ipsilateral to the lesion. (An over-stepping or goose-stepping gait with a delayed onset of voluntary motion which, when initiated, is exaggerated.) Spasticity ipsilateral to the lesion without paresis/paralysis	A broad-based stance, swaying of the body from side to side and a tremor of the head and neck, most noticeable when fine movements are required. Dysmetric, spastic postural reactions ipsilateral to the lesion	Normal	Normal	An absent menace response, although the eye appears able to see, ipsilateral to the lesion. Off-balance, head tilt, nystagmus and strabismus	Intention tremor. Truncal ataxia

9.1 Clinical signs of neurological diseases. (continues)

▶

Mental status	Gait	Postural ability	Segmental reflexes	Sensation	Cranial nerve function	Other
Cervical spinal cord segments 1–5 (C1–C5)						
Normal	Ataxia and spastic hemi- or tetraparesis/ paralysis	Ipsilateral or bilateral postural reaction deficits and increased extensor tone of the limbs	Ipsilateral or bilateral hyperreflexia of the limb reflexes	Decreased at and below the level of the lesion	No abnormalities	Cervical muscle spasms. Horner's syndrome (uncommon). Respiratory muscle paresis/ paralysis. Urinary incontinence and decreased ability to express the bladder
Cervical spinal cord segment 6 to thoracic spinal cord segment 2 (C6–T2)						
Normal	Hindlimbs: ipsilateral or bilateral ataxia and spastic paresis/paralysis Forelimbs: ipsilateral or bilateral flaccid paresis/ paralysis	Hindlimbs: ipsilateral or bilateral postural reaction deficits and increased extensor tone of the limbs Forelimbs: ipsilateral or bilateral postural reaction deficits and decreased extensor tone of the limbs	Hindlimbs: ipsilateral or bilateral hyperreflexia of the limb reflexes Forelimbs: ipsilateral or bilateral hyporeflexia of the limb reflexes	Decreased at and below the level of the lesion	No abnormalities	Horner's syndrome ipsilateral to the lesion. Diaphragmatic breathing. Ipsilateral or bilateral depressed cutaneous trunci reflex. Urinary incontinence and decreased ability to express the bladder
Thoracic spinal cord segment 3 to lumbar spinal cord segment 3 (T3–L3)						
Normal	Hindlimbs: ipsilateral or bilateral ataxia and spastic paresis/paralysis Forelimbs: normal	Hindlimbs: ipsilateral or bilateral postural reaction deficits and increased extensor tone of the limbs Forelimbs: normal	Hindlimbs: ipsilateral or bilateral hyperreflexia of the limb reflexes Forelimbs: normal	Decreased at or below the level of the lesion	No abnormalities	Schiff–Sherrington posture. Urinary incontinence and decreased ability to express the bladder
Lumbar spinal cord segment 4 to sacral spinal cord segment 1 (L4–S1)						
Normal	Hindlimbs: ipsilateral or bilateral flaccid paresis/ paralysis Movement is characterized by scuffing the paws; a stiff, short-strided gait; or inability to support weight Forelimbs: normal	Hindlimbs: ipsilateral or bilateral postural reaction deficits and decreased extensor tone of the limbs Forelimbs: normal	Ipsilateral or bilateral hyporeflexia of the hindlimbs	Decreased at or below the level of the lesion	No abnormalities	Schiff–Sherrington posture. Urinary incontinence and decreased ability to express the bladder
Sacral spinal cord						
Normal	Hindlimbs: normal gait or ipsilateral or bilateral scuffing of the paws Forelimbs: normal	Hindlimbs: normal or ipsilateral or bilateral plantigrade posture Forelimbs: normal	Normal or hyporeflexive sciatic nerve reflexes. Decreased anal sphincter tone. Depressed bulbocavernosus reflex	Decreased sensation of the perineal area, tail and skin over the limb innervated by the sciatic nerve	No abnormalities	Urinary incontinence with an easily expressible bladder

9.1 (continued) Clinical signs of neurological diseases. (continues)

▶

Mental status	Gait	Postural ability	Segmental reflexes	Sensation	Cranial nerve function	Other
Peripheral nerves						
Normal	Monoparesis, hemiparesis or tetraparesis. Movement is characterized by scuffing the paws; a short-strided gait; or inability to support weight	Postural reaction deficits and decreased extensor tone of the affected limbs	Hyporeflexia in affected limbs. Decreased anal tone	Normal or decreased sensation of affected regions	Decreased sensation of the face, decreased jaw tone, masticatory muscle atrophy (CN V); decreased palpebral reflex (CN V and VII); medial strabismus, decreased globe retraction (CN VI); drooping lips, inability to blink the eyelids or move the ears (CN VII); nystagmus, head tilt and positional ventral strabismus (CN VIII); dysphagia, dysphonia, decreased gag reflex (CN IX and X); regurgitation, megaoesophagus (CN X); decreased tongue motion and tongue muscle atrophy (CN XII) ipsilateral to the lesion	Urinary incontinence with an easily expressible bladder. Faecal incontinence. Quickly progressing and severe muscle atrophy. Exercise intolerance. Possible hypoventilation
Skeletal muscle						
Normal	Monoparesis, hemiparesis or tetraparesis. Movement is characterized by scuffing the paws; a short-strided gait; or inability to support weight	Postural reaction testing may be normal if the animal is supported; however, postural reaction deficits may occur in affected limbs	Normoreflexia or hyporeflexia in affected limbs. Decreased anal tone	Normal, or muscle may be painful on palpation	Decreased jaw tone; ipsilateral or bilateral masticatory muscle atrophy; drooping lips; decreased ability to blink or to move the ears; dysphagia; dysphonia; decreased gag reflex; regurgitation; megaoesophagus; decreased tongue motion with atrophy of the tongue muscle	Quickly progressing and severe muscle atrophy. Exercise intolerance. Limited joint motion

Spinal cord disorders result in no abnormalities of mental status or cranial nerve function. Deficits in gait, postural ability, reflexes and sensation occur at or caudal to the level of the lesion and ipsilateral to the lesion. Bilateral deficits may occur if the lesion crosses the midline of the spinal cord.

- **Ataxia:** incoordination; may be characterized by crossing over of the limbs, increased stride length, abduction or circumduction of a limb or limbs, walking on the dorsum of the paw, or the failure of an observer to predict where a paw will land.
- **Dysmetria:** a form of ataxia, characterized by abnormal rate or range of movement.
- **Paresis:** partial loss of voluntary motor ability; may be characterized by an inability to support weight fully while walking or standing, scuffing of the paws when walking and tremoring when trying to stand.
- **Paralysis:** complete loss of voluntary motor ability.
- **Spasticity:** increased extensor tone of the limbs.
- **Abnormalities associated with hypothalamic involvement:** diabetes insipidus, diabetes mellitus, hyperadrenocorticism and acromegaly; abnormalities in appetite, thirst, sleep, sexual behaviour, temperature regulation and electrolyte regulation.
- **Cheyne–Stokes pattern of respiration:** a repeating pattern of deep and shallow respiration followed by periods of apnoea.
- **Horner's syndrome:** miosis, ptosis, prolapsed third eyelid and enophthalmosis.
- **Schiff–Sherrington posture:** characterized by increased extensor tone and normal postural ability of the forelimbs.
- **Bulbocavernosus reflex:** squeezing the bulb of the penis or the vulva causes contraction of the anal sphincter in normal animals.

9.1 (continued) Clinical signs of neurological diseases.

Brainstem disease

Destructive brainstem disease: Neoplasia and encephalitis of the brainstem may result in an acute or progressive onset of brainstem dysfunction. Chemotherapy, antimicrobials/antifungals or anti-inflammatories may be required. Trauma and haemorrhage in the brainstem may also result in acute onset of dysfunction. Traumatic brainstem haemorrhage or thrombosis is treated by support of the patient with careful monitoring. When haemorrhage is due to an underlying coagulopathy this should be treated specifically if possible, while thrombosis might require anticoagulant therapy (see Chapter 13).

Herniation: Neoplasia, inflammation (e.g. canine distemper virus, granulomatous meningoencephalitis, necrotizing encephalitis, feline infectious peritonitis, toxoplasmosis/neosporosis, mycotic diseases) or trauma of the cerebral hemispheres may result in increased ICP, unilateral or bilateral occipital lobe herniation and brainstem compression. Herniation is often preceded by hours to days of progressive cerebral hemisphere/diencephalon dysfunction, including progressive depression of consciousness. Occipital lobe herniation is suspected if there is development (over hours to days) of unilateral or bilateral non-responsive dilated or mid-position pupils, progressive loss of physiological nystagmus, and alterations in respiratory patterns.

Interestingly, significant occipital lobe herniation can occur even in the absence of clinical signs (Walmsley *et al*., 2005). Herniation of the cerebellum through the foramen magnum may result in apnoea. Increases in ICP causing herniation should be treated without delay by the methods discussed in the section on head trauma.

Metabolic causes

Metabolic disease and toxins rarely result in neurological deficits that indicate discrete lesions of the nervous system. Rather, bilaterally symmetrical deficits that suggest diffuse cerebrocortical dysfunction or diffuse brain disease are usual. Signs are often progressive. Evidence of vision is present until stupor is profound or coma occurs. Pupils are responsive and usually of normal diameter but may be bilaterally miotic. Physiological nystagmus is generally present unless profound stupor or coma occurs. Metabolic causes for stupor or coma include diabetic coma, hepatic encephalopathy, hypo- and hypernatraemia, hypoglycaemia, hypothyroid coma, hypoxia, renal encephalopathy and thiamine deficiency (see below). Toxic causes include heavy metals, ethylene glycol, barbiturates, narcotics, ivermectin and tranquillizers. Intoxication is treated by gastric lavage, activated charcoal, specific antidotes and chelating agents, and by support of the patient (see Chapter 19).

Vascular causes

Stupor or coma may result from infarction/haemorrhage of the midbrain, or from infarction/haemorrhage in the cerebral hemispheres and diencephalon, resulting in increased ICP and occipital lobe herniation. Causes of cerebrovascular accidents in animals include trauma, metastatic neoplasia, coagulation disorders, cardiac disease, hypertension, parasitic emboli and feline ischaemic encephalopathy, although an underlying cause is not usually identified. In a study of 33 dogs with brain infarction, a concurrent medical condition was found in only just over half the dogs (Garosi *et al*., 2005). Predisposing vascular disease, common in humans, is rare in animals. If vascular disease is suspected the following diagnostics should be considered: cardiology evaluation, coagulation screens, endocrine testing, serial blood pressure measurement and evaluation for metastatic disease. Infarction is treated by supporting the patient, treating any underlying disease and decreasing ICP.

Head trauma

A global assessment of the patient must be performed, paying specific attention to ensuring that the airway is patent, providing respiratory support if necessary and maintaining cardiovascular function. Ideally, the initial assessment should be performed on a board or firm table where the neck and back can be immobilized and assessed for fractures or luxations. Manipulation for radiography of any suspicious areas should be done with care. The nasal cavity, ear canals and nasopharyngeal region should be examined for haemorrhage, which may imply a skull fracture with the possibility of entry of bacteria into the brain. The jugular vein should not be used to collect blood since even temporary occlusion may increase ICP.

Neurological assessment

In general, trauma to the cerebral hemispheres causes less severe neurological dysfunction and a better prognosis than trauma to the brainstem. Trauma to the cerebellum alone is uncommon.

The progression of clinical signs over time plays a large role in determining prognosis. In humans, the Glasgow Coma Scale is used to classify traumatic brain injury into mild, moderate and severe, as well as to provide associated prognosis. A modified veterinary version of the scale with associated prognosis scores patients from a guarded prognosis (1) to good (18) (Shores, 1983). A retrospective study of 38 dogs evaluated the prognostic value of this modified Glasgow Coma Scale. The score of the patient was found to predict the probability of survival in the first 48 hours after head trauma in an almost linear fashion and with 50% probability of survival in patients with a score of 8 (Platt *et al*., 2001).

Deterioration of mental status may indicate increasing ICP and the possibility of impending brain herniation, therefore immediate therapeutic intervention is necessary. Prolonged (greater than 48–72 hours) stupor or coma suggests severe brainstem disease and indicates a poor prognosis. In general, pupillary abnormalities which become normal over time are a good prognostic sign; pupils which change to mydriasis or to mid-position and are unresponsive to light, and loss of normal physiological nystagmus are poor prognostic signs indicating oedema, herniation and compression of the brainstem, warranting more aggressive intervention.

Progressive alterations in breathing patterns, or increases in mean arterial blood pressure accompanied by bradycardia, may indicate increases in ICP requiring immediate therapy.

Intracranial pressure

The objective of management of head trauma is to prevent the brain from undergoing any further insult due to ischaemia, inflammatory mediators or the effects of increased ICP. Findings indicative of raised ICP include papilloedema, abnormal pulsing of retinal vessels, depression,

stupor or coma, and elevated blood pressure with a low heart rate (the Cushing reflex). ICP is rarely measured directly in small animal patients, therefore, increased ICP is frequently suspected but rarely confirmed.

ICP is the pressure exerted by tissues and fluids within the cranial vault. In normal animals, ICP ranges between 5 and 12 mmHg. Three 'compartments' exist within the skull: brain parenchyma (80%), blood (10%), and cerebrospinal fluid (CSF) (10%). If ICP is to remain constant, an increase in the volume of one of these components must be accompanied by a decrease in the volume of one (or both) of the others. In most diseases affecting the brain, a volume increase occurs in one or more compartments. Most commonly, this is in the form of cerebral oedema that adds to the volume of brain parenchyma, although haemorrhage and hydrocephalus can also add to the volumes of blood and CSF, respectively. In the initial stages of an increase in intracranial volume, mechanisms exist to minimize the consequent rise in ICP, first by displacing CSF out of ventricles into the spinal subarachnoid space, and then by reducing the blood volume contained within cerebral vessels. However, once this initial compliance has been exhausted, small increases in volume of any compartment result in large increases in ICP in an exponential fashion.

A separate, but related, concept is that of cerebral perfusion pressure (CPP). CPP determines the cerebral blood flow (CBF) and therefore the delivery of oxygen and nutrients to brain tissue. CPP is defined by the following equation:

$$CPP = MAP - ICP$$

where MAP is mean arterial pressure.

In patients with MAP in the range 50–150 mmHg, ICP is maintained within normal limits by the phenomenon of pressure autoregulation: as blood pressure rises, vasoconstriction occurs to minimize the volume of blood within the cerebral vasculature and thus prevent increases in ICP. Conversely, if ICP rises, autoregulation of cerebral perfusion should result in an elevation of MAP in an attempt to maintain CPP. This increased MAP may then provoke a baroreceptor-mediated bradycardia, the so-called Cushing reflex. However, if ICP rises excessively, autoregulatory mechanisms may not be sufficient to compensate. This is especially true if there is a concurrent drop in MAP, leading to a drop in CPP and insufficient blood delivery to the brain, resulting in tissue hypoxia and ultimately necrosis of brain tissue. Importantly, in regions of the brain that have suffered significant trauma, these mechanisms do not function normally, and may fail even before ICP rises above the normal range.

Tissue hypoxia and necrosis result in a complex chain of biochemical events that culminate in progressive cerebral oedema, setting up a self-propagating spiral of rising ICP. In this situation, systemic blood pressure may rise and heart rate may fall, in a last-resort attempt to maintain cerebral perfusion. For this reason, it is vital to monitor the patient's blood pressure if there is concern about elevated ICP.

Treatment

The following treatment recommendations are important for the care of the closed head trauma patient (Bagley, 1996).

Elevate the head and neck at a 30-degree angle above heart level

The patient may be placed in lateral or sternal recumbency on a solid board and the board elevated at a 30-degree angle, thereby facilitating venous drainage from the cranial vault. It is important to avoid bending the neck when elevating the head. Make sure no blankets or bandages compress the jugular veins, which would decrease venous drainage. Avoid any manipulations that would compress the jugular veins, such as venepuncture or compression during manual restraint.

Similarly, any manipulation that precipitates coughing should be avoided because coughing may cause increased ICP.

Control of ventilation

Hyperventilation can rapidly decrease ICP because hypocapnia causes cerebral vasoconstriction, thereby decreasing CBF. Studies have revealed, however, that the clinical use of hyperventilation may be contraindicated (Obrist *et al*., 1984; Muizelaar *et al*., 1991; Fortune *et al*., 1995; Skippen *et al*., 1997). After cranial trauma, oxygen extraction is maximal and blood flow is the limiting factor for cerebral oxygen utilization. Cerebral vasoconstriction induced by hypocapnia should therefore be avoided because oligaemia might result in inadequate cerebral oxygen delivery. Assisted ventilation is recommended if P_aCO_2 (as determined by blood gas analysis, or inferred from capnography) is elevated, but the goal should be to maintain it within normal limits (35–45 mmHg).

For the same reasons, hypoxaemia must be avoided and positive pressure ventilation should be considered to maintain oxygenation if the patient is stuporous or comatose. If the patient is not stuporous and is stable, supplemental oxygen, in the form of nasal oxygenation or via an oxygen cage, may be provided.

Maintenance of cerebral and systemic perfusion

Hypotension, hypoxia and hypertension must be avoided. In order to maintain CPP, fluid therapy should be used to maintain MAP between 70 and 110 mmHg (see Chapters 3 and 4). Hypotension that is non-responsive to fluid therapy should be treated with inotropes or pressors as indicated. Hypertension due to excitement and pain may be addressed with sedation or analgesics. Occasionally, a comatose animal may present with hypertension and bradycardia (Cushing reflex) due to increased ICP; treatment should be aimed at decreasing ICP.

Furosemide and mannitol

Mannitol can rapidly decrease ICP by drawing water out of oedematous cells into the intravascular space by osmosis, and then inducing an osmotic diuresis. Its effect is greatest 30–60 minutes after administration, and lasts 2–4 hours. An intravenous dose of 0.5–1 g/kg of a 25% solution administered over 20 minutes can be repeated every 3–8 hours, with a maximum of three doses over a 24-hour period. Mannitol causes an initial expansion followed by a significant contraction of the intravascular volume, and is therefore contraindicated in patients with shock, hypotension, dehydration, congestive heart failure, anuric renal failure or pulmonary oedema. Serum electrolytes and osmolality should be monitored because of the potential for free water loss in the diuresis.

Furosemide (1–4 mg/kg i.v.) may be given as a bolus prior to administration of mannitol. The aim is to prevent an initial rise in ICP associated with the expanded intravascular volume that occurs immediately following mannitol administration. Furosemide should be avoided in hypovolaemic patients.

Hypertonic saline

Hypertonic saline (HTS) administration offers a second option for decreasing ICP by osmosis; it is also thought to reduce blood viscosity and induce endothelial cell shrinkage, improving cerebral blood flow. HTS administration causes an improvement in MAP without the delayed hypovolaemia that occurs following mannitol administration. A review and meta-analysis of the literature on HTS use in humans showed a better outcome with HTS over other medications no matter what the aetiology of the increased ICP, and no serious side effects when sodium concentrations were monitored and treated if necessary (Mortazavi *et al*., 2012). HTS (7.5% NaCl) is administered at 4 ml/kg of bodyweight as a slow intravenous bolus; typically it is used only once in a 24-hour period because of concerns about hypernatraemia if multiple doses are given.

Dehydration is a relative contraindication for HTS use.

Corticosteroids

Corticosteroids were initially recommended for use in traumatic brain injury in humans after successful treatment of brain tumours and intracranial surgery associated with their use in the early 1970s. At that time the theory of treating with a high-dose steroid protocol was to help reduce brain oedema and ICP and provide free radical scavenging. In 2004, a multicentre collaboration called the CRASH trial reported results from over 10,000 human patients treated for head trauma. It found no reduction in mortality with methylprednisolone given within 2 weeks of the injury. The risk of death within 2 weeks was actually higher in the group treated with corticosteroids (Roberts *et al*., 2004).

A Cochrane review of the use of corticosteroids for acute traumatic brain injury in 2009 identified 20 trials of steroids in human patients with head trauma and a similar increase in mortality associated with steroid treatment (Alderson and Roberts, 2005). Hyperglycaemia is often present in head trauma patients and may be worsened by a treatment with corticosteroids. In dogs and cats, blood glucose concentration was found to be significantly associated with severity of head trauma but not associated with outcome (Syring *et al*., 2001). Elevated blood glucose has been associated with increased mortality in humans (Jeremitsky *et al*., 2005). Hyperglycaemia is thought to cause an increase in anaerobic glycolysis. As a result, there is an increase in lactic acid production, which causes further damage to the injured brain. Other proposed mechanisms include hyperosmolarity, alterations in neuronal pH and excitatory amino acids. The use of corticosteroids for head trauma patients is not part of the current standard of care at the authors' hospital.

Craniotomy

Craniotomy produces a rapid decrease in ICP and may be performed when managing skull fractures with a depressed displacement of bone more than the thickness of the calvarium in the fractured area, to remove projectiles, or to treat progressive increases in ICP that are refractory to medical management. In the future, the routine availability of ICP monitoring and computed tomography (CT) may aid in determining when craniotomy is necessary for the management of head trauma in dogs and cats.

Anaesthetic concerns

In patients with intracranial disease that require anaesthesia, the drugs chosen should not increase ICP or cause large changes in blood pressure, and should maintain adequate cerebral perfusion. Premedication may be limited to use of an intravenous benzodiazepine immediately prior to induction. This minimizes the required dose of induction agents and their respiratory and cardiovascular effects. In trauma patients, adequate pain control is essential in preventing further ICP elevation. The addition of an opioid in painful patients with no evidence of increased ICP (or low-dose opioid if there is suspected ICP elevation while attempting to reduce ICP) may help to provide pain control and maintain anaesthesia. When carefully titrated to the needs of the patient, opioids are an attractive analgesic because of their relative lack of cardiovascular effects and ease of reversal. Coughing at the time of intubation may raise ICP, and lidocaine (2 mg/kg i.v.) may be given for its antitussive effect immediately before intubation. Isoflurane is the maintenance agent of choice, because cerebral autoregulation is preserved if the inspired concentration is <1.0 x MAC (minimum alveolar concentration). When inhalants are contraindicated or insufficient, supplemental agents such as fentanyl or propofol may be used. During anaesthesia, end-tidal carbon dioxide monitoring (or blood gas analysis) coupled with intermittent positive pressure ventilation (IPPV) is important to maintain arterial carbon dioxide levels within normal limits of 35–45 mmHg. Hyper- or hypoventilation must be avoided (Greene, 2010).

Ketamine has the potential to reduce ischaemic injury by preventing NMDA (*N*-methyl-D-aspartate) receptor binding. It has also been demonstrated to reduce ICP in humans under propofol sedation. However, it has also been demonstrated to increase cerebral oxygen consumption. As there is no conclusive evidence for or against the use of ketamine in head trauma patients, the authors prefer to use other agents with more predictable results.

Alpha-2 agonists (dexmedetomidine) are commonly considered medications in general practice. Although there is little influence on ICP in patients, there is considerable reduction in heart rate and cardiac output, and this may impair cerebral perfusion. They should only be used at low doses (1–2 μg/kg/h) and only if other medications listed above are not available.

Sedation

Frequently, trauma-related pain or agitation may result in the patient flailing or constantly vocalizing; both behaviours may increase ICP. Diazepam (0.2–0.5 mg/kg) or phenobarbital (5 mg/kg) may be used to sedate the patient, potentially combined with butorphanol (0.2–0.4 mg/kg) or other narcotics, especially if the patient is thought to be in pain. Cardiorespiratory function must be carefully monitored. In the rare instance when these drugs do not result in a calm patient, small doses of acepromazine (0.01–0.02 mg/kg i.v.) may be given. Acepromazine has previously been implicated in reducing seizure threshold and inducing epileptiform activity in dogs. However, in a study of 36 dogs with seizure history, acepromazine was given for sedation with no evoked seizures. The medication was also administered to 10 actively seizuring dogs with an abatement of activity in eight dogs (Tobias *et al*., 2006).

Seizures and status epilepticus

Seizures result from a sudden uncontrolled discharge of neurons in the cerebral cortex or diencephalon. The manifestation of a seizure depends on the area and extent of the brain affected by the abnormal electrical activity. Primary generalized seizures occur when both cerebral hemispheres are affected. The patient may show symmetrical abnormalities of movement of the head and limbs (tonus, clonus, atony, myoclonus) with a loss of consciousness. Partial seizures occur when a group of neurons in a region of the cerebral cortex is affected. The patient shows signs indicative of stimulation of the cortical region: asymmetrical signs such as tonus or clonus of one or more limbs, turning the head and neck to one side, and twitching of one side of the face, or sudden changes in behaviour, may occur. Consciousness may or may not be affected and focal seizures may or may not progress to generalized seizures. Non-convulsive seizures or status epilepticus are episodes of abnormal electrical activity without tonic or clonic activity and are identified by electroencephalography (EEG).

The term 'epilepsy' means recurrent seizures. Epilepsy may be classified into three categories according to its cause: idiopathic, symptomatic and cryptogenic (Berendt and Gram, 1999).

Idiopathic epilepsy (IE) is the consequence of intrinsic chemical abnormalities that are not associated with structural cerebral pathology or extracranial disease. It is characterized by predominantly generalized seizures that typically begin between 6 months and 5 years of age. The animal is neurologically normal during the interictal period. A hereditary cause is presumed. Breeds with a high prevalence of epilepsy have been identified and investigated for a genetic or familial basis for seizures; these include the Belgian Shepherd Dog and Tervuaren, Beagle, Bernese Mountain Dog, Border Collie, Dalmatian, English Springer Spaniel, German Shepherd Dog, Irish Wolfhound, Golden and Labrador Retriever, Keeshond, Standard Poodle and Vizsla (Ekenstedt *et al*., 2012). A specific mutation in *LGI2*, an ortholog of the human epilepsy gene, has been found in the Lagotto Romagnolo and is responsible for the familial juvenile epilepsy in this breed (Seppala *et al*., 2011).

Symptomatic (secondary) epilepsy occurs when structural disease of the brain (brain tumours, encephalitis, malformations, sclerosis or trauma) provokes seizures. It is characterized by partial or generalized seizures that may begin at any age. The animal frequently, but not always, has neurological deficits that are recognized during the interictal period. A comparison report of 240 dogs with seizures showed that if the seizure occurred between 1 and 5 years of age IE was more likely. In total, 48% of the 240 dogs had IE, while 16% had intracranial neoplasia and 11% had encephalitis. Symptomatic epileptic dogs in this study (those with structural disease) were more likely to have interictal deficits, status epilepticus and cluster and partial seizures (Pakozdy *et al*., 2008).

The term cryptogenic epilepsy is used to designate recurrent seizures for which a symptomatic cause is suspected but has not been found. It is suspected when an animal has partial seizures, but brain imaging does not reveal a structural cause for the seizures. In a recent study of 212 seizuring dogs, 21% of dogs 7 years or older matched the definition of cryptogenic epilepsy, and seizure control was acceptable for most dogs (Schwartz *et al*., 2013). Single or recurrent seizures can also occur due to extracranial disease in which the normal brain is stressed by metabolic or toxic abnormalities (e.g. hepatic encephalopathy, uraemic encephalopathy, hypoglycaemia, hypocalcaemia, polycythaemia and toxins) (Podell *et al*., 1995). These have been referred to as reactive seizures.

Obtaining a good history

When presented with a patient having seizures the goals are:

- To confirm that the event is/was a seizure
- To stop the seizure and treat primary or secondary metabolic derangements
- To determine the cause of the seizure.

Confirmation that a seizure has occurred is based on the owner's description of the event or observation of the event by the veterinary surgeon (veterinarian) (either directly or by observing a recording). Non-convulsive seizures and sudden changes in behaviour present the most difficulty in determining whether or not a seizure has occurred. Differential diagnoses must include syncope, cataplexy, narcolepsy and behavioural disorders. While EEG can be used to confirm epileptiform activity in the brain, it is not routinely performed due to either the lack of equipment or the need for sedation.

The following questions may be asked of the client while assessing the patient.

- What did the seizure look like? What did the animal look like immediately before and immediately following the seizure? The presence of pre- or post-ictal signs may help confirm that a seizure has occurred and may suggest a structural cause if a partial seizure is described.
- Is the animal vaccinated?
- Has there been any exposure to toxins? Strychnine, lead, mercury, metaldehyde, moulds, organophosphates, chlorinated hydrocarbons, ethylene glycol, amphetamines, caffeine, theobromine, cocaine, 5-fluorouracil, ivermectin and others may cause seizures.
- Has the animal had seizures in the past? Is the animal currently taking anticonvulsants? How many seizures have occurred within the past year, 6 months or month? Generalized seizures occurring infrequently over years suggest IE or a static, structural lesion.
- How old is the animal? The onset of seizures in dogs due to IE is principally between 6 months and 5 years of age. IE is uncommon in cats.
- What time of day did the seizure occur? Seizures following feeding may be associated with hepatic encephalopathy. Seizures occurring when a meal has been missed, soon before a meal or associated with exercise may indicate hypoglycaemia.
- Is the animal neurologically normal between seizures? Animals with IE appear normal between seizures. Animals with symptomatic epilepsy may be normal between seizures or may be behaviourally abnormal, dull, circle, or show other signs of nervous system disease. These animals may also show signs of systemic disease.

Clinicopathological testing

Ideally, blood should be drawn for analysis prior to initiating therapy. It is recommended that a complete blood count, blood smear evaluation for inclusion bodies (seen

with canine distemper virus infection) and nucleated red cells (seen with lead toxicity), urinalysis and blood gas measurements be performed. Levels of serum electrolytes (Na, K, Ca, P, Mg), blood glucose, alanine aminotransferase, alkaline phosphatase, bilirubin, albumin, cholesterol, serum ammonia, blood urea nitrogen and serum creatinine should be determined. Additional serum may be refrigerated for future determination of anticonvulsant, insulin, thyroid hormone or bile acid concentrations, or for antibody titres for infectious diseases.

Seizures due to metabolic causes require specific therapy in addition to anticonvulsant medications (see Abnormal mental status and Metabolic encephalopathies for the treatment of hypoglycaemia, hypocalcaemia and thiamine deficiency).

Status epilepticus and cluster seizures may result in hypoxia, acidosis and/or hyperthermia, which require specific treatment. Seizures commonly result in hyperglycaemia. Rarely, however, prolonged status epilepticus may result in hypoglycaemia and the patient may require supplementation with dextrose.

Treatment

If the seizure lasts less than 2 minutes and is not repeated, no medication is required.

Seizures longer than 2 minutes, seizure clusters or status epilepticus

Cluster seizures are two or more seizures occurring over a 24 hour period. Status epilepticus is defined as a seizure that lasts longer than 5 minutes, or recurrent seizures without recovery of full consciousness between seizures. Initial treatment recommendations include:

- **Diazepam:** 0.2–0.5 mg/kg i.v. or 0.5–1.0 mg/kg rectally, may be repeated 2–3 times over 5–10 minutes
- **Midazolam** is a suitable substitute for diazepam: 0.1–0.5 mg/kg i.v.
- **Phenobarbital:** a total loading dose of 16 mg/kg i.v. is given divided into 3 or 4 doses over several hours. It may take up to 30 minutes before an effect is noted. If the animal is currently on an adequate dose of phenobarbital, there is little evidence that increasing the dose by another 16 mg/kg has any beneficial effect
- **Levetiracetam:** 20–60 mg/kg i.v. given every 8 hours. Recent work shows that serum levels in the human therapeutic range can be achieved with rectal administration of 40 mg/kg of an injectable solution (Peters *et al*., 2014)
- **Potassium bromide:** may be loaded by giving a total of 400–600 mg/kg orally divided into twice daily doses over 2–3 days. Gastrointestinal upset can occur with administration. Transient sedation and pelvic limb weakness can occur.

Benzodiazepines, levetiracetam, potassium bromide and phenobarbital may be given concurrently.

If status epilepticus or cluster seizures continue, one of the following regimens may be used:

- Intravenous constant rate infusion (CRI) of diazepam or midazolam administered at a rate of 0.1–0.5 mg/kg/h in a 5% dextrose solution
- Intravenous administration of 10–20 mg/kg thiopental (given as 2–4 mg/kg boluses to effect), and endotracheal intubation with or without isoflurane anaesthesia
- Intravenous administration of 2–6 mg/kg pentobarbital. This drug may lead to prolonged anaesthesia. Although a total dose of up to 15 mg/kg can be used, this should be administered as small boluses of 2–3 mg/kg. There should be at least 15 minutes between these boluses due to the prolonged nature of the drug's effects. Pentobarbital has very limited availability in a suitable formulation, and non-suitable formulations such as non-sterile multi-use bottles should only be used with careful consideration of the risk:benefit
- Intravenous administration of 6 mg/kg propofol (given as 1–2 mg/kg boluses to effect), followed by an intravenous CRI of propofol at 0.1–0.2 mg/kg/min. Propofol stops the outward signs of seizures; however, the authors have found that some dogs continue to have EEG evidence of status epilepticus while receiving propofol. If EEG monitoring is available it should be used; if it is unavailable the clinician should be aware that seizure activity may be continuing despite cessation of motor activity.

When intermittent dosing of benzodiazepine, levetiracetam and phenobarbital does not control seizures and any of the above protocols are used, profound sedation may result. The patient's gag reflex should be monitored, along with indices of oxygenation, ventilation, electrocardiogram and blood pressure. Endotracheal intubation and support of respiratory and cardiovascular status may be required. The patient should be anaesthetized for 15–30 minutes with propofol or thiopental. If seizures continue after recovery from anaesthesia, repeated anaesthesia for longer periods of time may be attempted.

Maintenance medication

- Phenobarbital (3–5 mg/kg orally q12h). Serum concentration attains a steady state within 2 weeks.
- Or potassium bromide (30–40 mg/kg orally q24h). Serum concentration attains a steady state in 2–4 months.

Third-line medications are now widely available and generic versions are affordable:

- Levetiracetam (20–40 mg/kg orally q8h). Serum concentration testing is available, but there is no defined therapeutic level for small animals
- Zonisamide (5–10 mg/kg orally q12h). If the patient is on phenobarbital the maintenance dose is started at 10 mg/kg to overcome induced liver metabolism.

Prognosis

Idiopathic epilepsy is rarely life-threatening unless status epilepticus develops. However, blindness, weakness, or changes in behaviour may continue for days or weeks following a seizure and may be made temporarily worse by anticonvulsant medications. If status epilepticus does occur, it is important to treat secondary problems such as hyperthermia, metabolic disturbances, aspiration pneumonia, acid–base imbalance and myoglobinuria.

Animals with symptomatic epilepsy require further diagnostic testing including CSF analysis and brain imaging. If symptomatic epilepsy is suspected, medication in addition to anticonvulsants may be required (e.g. mannitol, steroids, antifungals, antibacterials). Animals with reactive epilepsy require treatment of the underlying metabolic disease.

Abnormal mental status

Abnormal mental status may result from disease of the cerebral hemispheres or brainstem, with the most common emergency presentations being due to encephalitis, neoplasia or metabolic encephalopathies.

Encephalitis

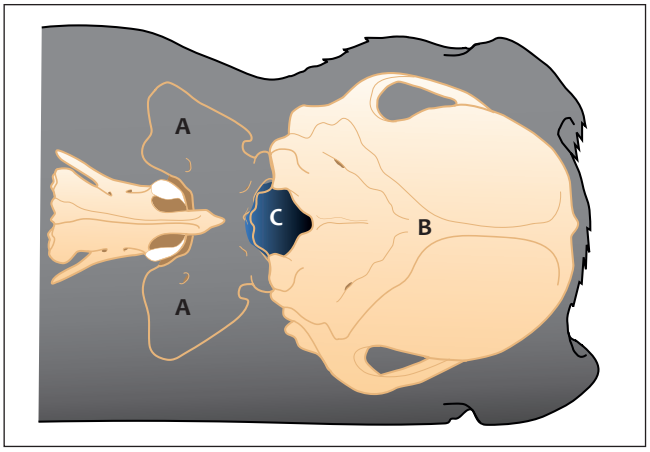
Common causes of encephalitis in dogs include steroid-responsive meningitis/arteritis, protozoal diseases (*Toxoplasma*, *Neospora*), canine distemper virus, inflammatory diseases in which no aetiological agent can be identified (meningoencephalitis of unknown aetiology, granulomatous meningoencephalitis (GME), necrotizing encephalitis) and, in some locations, rickettsial diseases (Rocky Mountain spotted fever, *Ehrlichia*) and fungal diseases (*Cryptococcus*, *Blastomyces*, *Aspergillus*). In cats, feline infectious peritonitis, feline immunodeficiency virus, *Toxoplasma* and fungal disease are the most common causes of encephalitis.

Animals with encephalitis are commonly depressed or disorientated, and a recent onset of seizures is common. Evidence of systemic disease is useful in making a tentative diagnosis of some causes of encephalitis but two of the more common causes, GME and necrotizing encephalitis, are typically not associated with extracranial disease. Examination of the ocular fundus is strongly recommended, since ocular disease occurs commonly with some encephalitides (canine distemper virus, *Toxoplasma*, *Cryptococcus*, feline infectious peritonitis) and since the presence of papilloedema is supportive evidence for increased ICP.

It is useful to submit titres for infectious diseases, but the results of these tests may not be available for several days. CSF analysis may reveal fungal organisms (occasionally) or inclusion bodies (rarely) but more commonly shows inflammation without evidence of aetiology. CSF is readily collected under general anaesthesia at the cerebellomedullary cistern using a spinal needle (Figures 9.2 and 9.3). Normal CSF protein is <0.25–0.3 g/l and normal cellularity is <5 white blood cells per microlitre. Some CSF analysis findings support specific diagnoses; for example, a mononuclear pleocytosis with mild to moderate increases in protein is consistent with GME, necrotizing encephalitis and lymphoma. Moderate increases in neutrophils in addition to mononuclear cells may be seen with GME, toxoplasmosis, neosporosis and fungal disease.

1. Place the animal in lateral recumbency under general anaesthesia.
2. Clip the skin and prepare for an aseptic procedure.
3. Flex the head to 90 degrees and have an assistant hold it in place.
4. The occipital protruberance and the spinous process of C2 are palpated; an imaginary line is drawn through these two points; this line should be parallel to the table surface (if not, the nose is either raised or lowered).
5. The most rostral extents of the wings of the atlas are palpated and an imaginary vertical line is drawn between the two wings.
6. A 20 or 22 G CSF needle is inserted parallel to the table surface and parallel to the nose, on the midline of the patient, halfway between the occipital protruberance and an imaginary line between the wings of the atlas (see Figure 9.3).
7. The needle should be held securely and slowly advanced. The stylet is removed every 5 mm or so to look for fluid. Once fluid is seen in the hub of the needle, it is held in place while the sample is collected.
8. The needle should not be redirected once it has entered the muscle as side-to-side motion of the needle can damage the spinal cord.

9.2 Method for cerebrospinal fluid tap.



9.3 Anatomical landmarks for atlanto-occipital CSF collection. A = wings of the atlas vertebra; B = occipital protruberance; C = site of fluid sampling.

Marked increases in neutrophils are common with feline infectious peritonitis and steroid-responsive meningitis/arteritis. Moderate to marked increases in eosinophils can be seen with parasitic diseases, protozoal diseases and eosinophilic meningitis.

When encephalitis is suspected, the clinician must frequently institute therapy prior to obtaining a definitive diagnosis through titres or biopsy. Emergency therapy should therefore be directed at the most common causes of encephalitis found in the geographical region. For example, in the Philadelphia region in the USA, treating dogs with doxycycline and prednisolone is common, due to the prevalence of Rocky Mountain spotted fever, GME and necrotizing encephalitis in the patient population. Mannitol may also be required to treat increases in ICP. When a definitive diagnosis is made, therapy is altered to treat the specific cause.

Neoplasia

Primary intracranial neoplasia is one of the most common causes of altered mental status and seizures in older patients (Troxel *et al*., 2003; Snyder *et al*., 2006). Definitive diagnosis in an emergency setting may be hindered by the absence of advanced imaging capabilities. A CSF analysis showing a significant increase in protein without a significant increase in cellularity (albuminocytological dissociation) is supportive but not definitive for intracranial neoplasia. When neoplasia is suspected, the animal may be treated with steroids to decrease vasogenic oedema and mannitol to decrease ICP, until the brain can be imaged with CT or magnetic resonance imaging (MRI).

Metabolic encephalopathies

Metabolic encephalopathies result in seizures, bilaterally symmetrical signs of cerebrocortical dysfunction, or signs of diffuse brain disease. Abnormalities of mental status may progress to stupor and coma (see Loss of consciousness and coma). History and bloodwork are essential in determining that the signs are due to metabolic disease. However, CSF analysis, titres for infectious disease and brain imaging are frequently necessary to rule out other causes of encephalopathy.

Calcium

Hypocalcaemia (total calcium <1.6 mmol/l; ionized calcium <0.6 mmol/l) may cause muscle twitching and spasms,

disorientation, restlessness and seizures. Intravenous administration of 10% calcium gluconate (50–150 mg/kg) over 15 minutes, followed by calcium gluconate diluted in saline and given subcutaneously (50–150 mg/kg q6–8h; Feldman, 2005) or 10 mg/kg/h i.v. by CRI often resolves clinical signs until the specific cause is identified.

Hypoglycaemia and hypomagnesaemia may occur concurrently and supplementation may be necessary. Diazepam may be necessary to control seizures.

Hypercalcaemia (total calcium >3.0 mmol/l) may cause muscle weakness, seizures, depression, stupor or coma. Diuresis with intravenous 0.9% sodium chloride and furosemide may be performed until the cause is determined (for more information, see Chapter 5).

Sodium

Both hyper- and hyponatraemia may cause neurological signs, with the severity of the signs being most dependent on the rapidity of onset of the change in sodium as opposed to the actual serum value. Severe hyponatraemia (Na^+ <120 mmol/l) may cause disorientation, seizures, stupor or coma. Ideally, plasma sodium concentration is corrected at the rate at which it was lost, i.e. acute decreases in plasma sodium may be corrected quickly, while chronically low sodium concentrations should be gradually increased at a rate no greater than 0.5 mmol/l/h. Excessively rapid correction of chronic hyponatraemia (>10 mmol/l/day) may cause weakness, hypermetria, ataxia and myoclonic jerking of the limbs 3–5 days after treatment (O'Brien *et al*., 1994).

If hypernatraemia (Na^+ >170 mmol/l) occurs acutely, restlessness, irritability, seizures, stupor and coma may occur. If hypernatraemia is chronic, only depression and disorientation may be noted. Chronic hypernatraemia must be treated slowly, at a correction rate no greater than 0.5 mmol/l/h (over 2–3 days) to avoid cerebral oedema. Further details can be found in Chapter 5.

Glucose

Hypoglycaemia (blood glucose <2.5 mmol/l) may cause weakness, muscle tremors, blindness, seizures, stupor or coma. Intravenous administration of 0.5 g/kg of 10–25% dextrose solution may be given until signs resolve. Anticonvulsants may be necessary to control seizures. When an insulin-secreting tumour is present, dextrose (by CRI), diazoxide (10 mg/kg q12h) and prednisolone (0.5 mg/kg q24h) are often necessary to maintain serum glucose concentrations.

Hyperglycaemia and hyperosmolality (>340 mOsm/l) may cause stupor and coma. Sodium chloride 0.45–0.9% or balanced electrolyte replacement solutions administered intravenously and insulin may be given to gradually correct hyperglycaemia over 24–36 hours and reduce the risk of cerebral oedema. Potassium supplementation should be provided (see Chapter 16).

Heat stroke

A body temperature of >41°C may result in blindness, ataxia, disorientation, stupor or coma. Cooling and hydrating the patient and correcting any acidosis, hypoglycaemia, hypernatraemia, hypokalaemia, hypophosphataemia and hypocalcaemia are recommended. If neurological dysfunction progresses, increased ICP may be present (see Head trauma for treatment).

Hepatic encephalopathy

Disorientation, pacing, blindness and circling often develop with hepatic encephalopathy; seizures, stupor and coma occur less commonly. Treatment is directed at decreasing the intake and absorption of protein-derived toxins from the large intestine (Bunch, 1995). Warm-water cleansing enemas and lactulose enemas retained for 20 minutes (20 ml/kg of 3 parts lactulose to 7 parts water) may be given every 4–6 hours. Neomycin sulphate (22 mg/kg orally q8h) or metronidazole (7.5 mg/kg orally or i.v. q8h) may be administered to decrease the bacterial load. Serum glucose and potassium concentrations should be monitored and deficits corrected. Hydration should be maintained. If present, gastrointestinal bleeding will lead to worsening of the signs and must be controlled; the presence of coagulopathy secondary to hepatic failure should be assessed.

Hepatic encephalopathy is associated with the presence of increased numbers of GABA receptors, and administration of GABA receptor antagonists such as flumazenil (20 μg/kg i.v.) may result in improved mental status in these patients.

Seizures occasionally occur after surgery for portosystemic shunt (PSS) ligation. These seizures are notoriously difficult to control with phenobarbital or diazepam. The use of potassium bromide or propofol has been more effective; however, the prognosis for many of these animals remains poor, and post-mortem examination has revealed severe cerebrocortical necrosis. A study of the incidence of postoperative seizures in dogs with PSS with and without pretreatment with levetiracetam showed promising results, with a significant reduction in seizures and death in dogs treated with the drug. No untreated dog that developed seizures survived the hospitalization (Fryer *et al*., 2011).

Hypoadrenocorticism

Depression, lethargy, weakness and shock may occur. Depending on the severity of signs, intravenous 0.9% saline, dexamethasone sodium phosphate (0.5–2.0 mg/kg), dextrose and/or sodium bicarbonate may be necessary (see Chapter 16).

Hypoxia and ischaemia

Changes in mental status, blindness and ataxia may occur with P_aO_2 values <55 mmHg, especially if hypoxia is also associated with decreased cerebral blood flow, for example following successful resuscitation from cardiopulmonary arrest. Treatment includes providing supplemental oxygen, treating the underlying cause of the hypoxia and if necessary providing mannitol to decrease cerebral oedema. Following successful resuscitation from arrest, blindness and changes in mental status will often resolve over weeks but may be permanent.

Lead poisoning

Whole blood lead concentrations >1.932 μmol/l may result in dementia and seizures, in addition to gastrointestinal signs. Chelation therapy with EDTA, D-penicillamine or succimer (10 mg/kg orally q8h for 10 days; Ramsey *et al*., 1996) are specific therapies for intoxication, along with removal of the source of lead if appropriate.

Renal encephalopathy

Severe uraemia due to acute renal failure may result in seizures. Chronic renal failure more commonly causes

mental dullness, weakness, muscle twitching and myoclonus. Treatment is aimed at monitoring blood pressure and maintaining hydration, acid–base status and electrolyte concentrations.

Thiamine deficiency

This is usually caused by a deficiency of dietary thiamine, through cooked food or a diet high in fish containing thiaminase. Clinical signs include signs of central vestibular disease, ataxia, ventroflexion of the head and neck, bilaterally dilated fixed pupils, and seizures, stupor and coma. Thiamine hydrochloride (10–20 mg/kg i.v.) is used to treat signs and repeated intramuscularly or subcutaneously daily until improvement is noted.

Thyroid hormone

Hypothyroidism (myxoedema crisis) may result in depression, disorientation, stupor or coma, most commonly in the Dobermann. Serum cholesterol concentrations >25 mmol/l may occur. Abnormalities are reversible with thyroid supplementation. Respiratory support, glucocorticoids and intravenous L-thyroxine may be necessary in cases of coma (Kelly, 1989).

Hyperthyroidism may cause restlessness, hyperexcitability, circling and seizures. Rarely, lethargy may occur. Treatment with methimazole, surgery or radioactive iodine resolves these signs. A low-iodine diet has also been developed for the treatment of cats with this condition.

Acute vestibular or cerebellar signs

Signs of vestibular system dysfunction which occur regardless of lesion location include:

- Ataxia characterized by falling due to loss of balance
- Abnormal posture characterized by leaning, turning of the head, neck and body and/or rolling head tilt. A head tilt exists when an imagined horizontal line running through both ears is tilted from the horizontal plane
- Ventral strabismus of the eye. The strabismus may not be noted until the head is elevated or returned to the horizontal plane
- Abnormal nystagmus.

Several techniques can be used to accentuate the clinical signs; for example, blindfolding the animal may accentuate the ataxia, lifting the animal off the ground may increase the head tilt and rolling and placing the animal on its back may induce nystagmus.

Compulsive circling (associated with disease of the cerebral hemispheres and diencephalon) should not be attributed to disease of the vestibular system. With compulsive circling there is no ataxia, no loss of balance and no abnormal nystagmus.

Localizing signs of vestibular system dysfunction

Vestibular system dysfunction may result from disease of the inner ear (often termed peripheral vestibular disease) or of the medulla or cerebellum (often termed central vestibular disease). The location of the lesion may be determined by the presence of neurological deficits in addition to those listed above.

Ear

Disease of the inner ear alone results in only the signs listed above. Auditory dysfunction is rarely recognized. The animal falls towards the side of the lesion and has a head tilt and strabismus ipsilateral to the lesion. The direction of the nystagmus is usually horizontal or rotatory, with the slow phase directed towards the side of the lesion and unchanged when the position of the head is altered. If the middle ear is also affected, signs of CN VII dysfunction and Horner's syndrome may result. No postural reaction deficits occur.

Medulla/cerebellum

Disease of the medulla may cause changes in mental status. Hemiparesis and postural reaction deficits and dysfunction of CN V–XII may occur ipsilateral to the lesion. The direction of the nystagmus may be horizontal, rotatory or vertical and may change when the position of the head is altered.

Disease of the cerebellum may cause dysmetria and menace deficits ipsilateral to the lesion, and head and neck tremors.

Exceptions to rules of localization

Bilateral peripheral vestibular disease may result in a wide-based stance and swaying of the body. There are wide excursions of the head to each side. Often, no abnormal nystagmus or strabismus is noted. The animal is typically severely ataxic when blindfolded or when lifted off the ground.

Occasionally, disease of specific sites within the cerebellum and medulla (flocculonodular lobe, caudal cerebellar peduncle) results in head tilt, strabismus and slow phase of the nystagmus directed away from the side of the lesion (paradoxical vestibular syndrome). The postural reaction deficits are ipsilateral to the lesion.

Causes and management of diseases of the vestibular system

Ear

Idiopathic labyrinthitis: Older dogs and cats of any age may be affected. CN VII dysfunction and Horner's syndrome do not occur. No abnormalities are found in blood, images of the bullae, deep otic examination or thyroid testing. Antibiotics are recommended if a full work-up for ear infection is not performed, but are not necessary to treat labyrinthitis, which is presumed to be of viral origin. Spontaneous recovery is common.

Otitis interna/media: Images of the osseous bullae and/or deep otic examination may confirm middle ear disease. Treatment with co-amoxiclav, cephalosporins, clindamycin, enrofloxacin or trimethoprim/sulfadiazine, with or without bulla osteotomy, is recommended. Extension of the infection into the cranium can occur. A study of 11 cats and 4 dogs with intracranial extension had a good/excellent prognosis with surgical exploration by ventral bulla osteotomy and appropriate antibiotic therapy (Sturges *et al*., 2008).

Other causes: Polyneuropathy, tumours, nasopharyngeal polyps and trauma involving the inner ear may result in vestibular system dysfunction. Hypothyroidism may be associated with polyneuropathy, and occasionally vestibular signs resolve only after the institution of thyroid hormone supplementation. Aminoglycosides at high doses may result in deafness and signs of peripheral vestibular dysfunction.

Medulla/cerebellum

Infectious/inflammatory diseases: Canine distemper virus, Rocky Mountain spotted fever, *Toxoplasma*, *Neospora*, *Cryptococcus neoformans*, GME, feline infectious peritonitis, parasitic migration and other meningoencephalitides may result in vestibular system dysfunction.

Neoplasia: This may be suspected on the basis of CSF fluid abnormalities and images of the brain. Tumours that can be found in this location include choroid plexus tumours, meningioma and medulloblastoma.

Toxicity: Metronidazole intoxication seen at doses greater than 30 mg/kg/day can result in an acute onset of vestibular system dysfunction with vertical nystagmus and, occasionally, seizures. Supportive care, requiring a week or more of hospitalization, results in recovery, although months may be required before all signs resolve. Recovery may be hastened by treatment with diazepam (Evans *et al*., 2002).

Metabolic: Thiamine deficiency may result in vestibular system dysfunction. Intramuscular thiamine hydrochloride (10–20 mg/kg i.v., i.m., s.c., continued until signs improve) can resolve the signs.

Vascular: Infarction of the medulla or cerebellum may be suspected on the basis of CSF abnormalities and images of the brain. In one study of 40 dogs with MRI diagnosis of infarct, 47% of the infarcts occurred in the cerebellum in the area of the rostral cerebellar artery (Garosi *et al*., 2006).

Dogs with cerebellar infarcts have acute signs of cerebellar ataxia, head tilt, opisthotonos, nystagmus and ipsilateral menace deficit with normal vision. The clinical signs are non-progressive and usually show initial improvement in 3–5 days.

Pelvic limb paresis and paralysis

Pelvic limb paresis and paralysis may result from a lesion between the third thoracic spinal cord segment and the first sacral spinal cord segment, as well as from diseases of peripheral nerve, muscle and neuromuscular junction.

Causes and management of diseases of the spinal cord

Intervertebral disc disease

Acute onset of neurological dysfunction and/or pain on palpation over the affected area may occur. Intervertebral disc protrusion/herniation may be confirmed by myelography, CT or MRI. Animals with pain and mild ataxia/paraparesis may be treated with strict cage confinement for 4 weeks.

Animals with moderate paraparesis or paraplegia but with intact nociception (assessed by looking for conscious recognition of compression of digits with haemostats or bone with bone forceps) may be treated either with strict cage confinement or surgical decompression, although there is a higher rate of recovery in animals treated surgically. Animals initially managed with cage confinement that then deteriorate should be treated surgically, since this may indicate further extrusion of the already-extruded disc. Animals with paraplegia and anaesthesia (i.e. lack of nociception) are a surgical emergency. If surgical decompression is performed within 24 hours of the onset of signs, there is an approximately 50% chance of significant recovery. These animals may be treated with methylprednisolone sodium succinate if seen within 8 hours of the onset of acute signs (30 mg/kg i.v.; then 15 mg/kg at 2 and 6 hours; then 2.5 mg/kg/h for 24–48 hours). However, there is considerable debate as to the efficacy of corticosteroids in this situation, surgical intervention is vital and potential adverse effects of high-dose corticosteroids should be considered.

Patients that are managed with cage confinement should initially be treated with analgesics. There is some evidence to suggest that the use of corticosteroids may be detrimental (Olby, 1999), and it is probably safer to use opioids initially, followed by a longer course of non-steroidal anti-inflammatory drugs (NSAIDs). If corticosteroids are used, prednisolone can be given at a dose of 0.5 mg/kg orally twice daily for 3 days, followed by 0.5 mg/kg once daily for 3 days, followed by 0.5 mg/kg every other day for 3 days. All patients should be treated with a gastroprotectant whether or not they receive corticosteroids or NSAIDs, as evidenced by a study of 30 dogs undergoing decompressive surgery for intervertebral disc disease that had an overall prevalence of ulceration of 76%, regardless of treatment with ulcerogenic medications preoperatively (Dowdle *et al*., 2003). In all cases, it is important to check neurological status regularly (at least twice daily), and if any worsening occurs surgery should be performed immediately.

Neoplasia

Neoplasia may result in a gradual or sudden onset of clinical signs. Imaging modalities confirm the presence and location of the mass from extradural, intradural extramedullary to intramedullary. Extradural tumours are the most common spinal tumours of dogs and cats (i.e. osteosarcoma, chondrosarcoma, multiple myeloma, lymphoma). Intradural extramedullary tumours include meningiomas and peripheral nerve sheath tumours. Intramedullary tumours are rarer but involve cells of the spinal cord parenchyma (astrocytoma, oligodendroglioma and ependymoma). CSF rarely contains neoplastic cells; however, examination of spinal fluid may raise suspicion of inflammatory disease. Biopsy yields a definitive diagnosis.

The most common spinal cord tumour of cats is lymphoma. These cats frequently also have disease present in extraneural locations (85% of cats in one study). They may be positive for feline leukaemia virus and often have lymphoblastic leukaemia on bone marrow aspiration (Spodnick *et al*., 1992). Signs due to spinal cord compression may respond to steroid therapy, and possibly decompressive surgery or radiation. Cage rest is recommended for animals with neoplasia associated with vertebral body lysis, due to the risk of pathological fracture (Bagley, 2010). Survival times vary depending on the tumour type and treatment with surgery, chemotherapy and/or radiation therapy and owner assessment of quality of life.

Discospondylitis

Fever, depression and pain over the affected area are common. Radiographs or bone scans may reveal lysis of the vertebral endplates; however, early in the course of the disease no abnormalities may be found. Culture of urine, blood or the affected disc may identify the causative organism. Treatment involves cage rest and antibiotics (cephalosporins, oxacillin, cloxacillin or tetracycline) for at least 6–8 weeks, although some recommend long-term therapy (Burkert *et al*., 2005).

Distemper, feline infectious peritonitis, mycotic/bacterial/protozoal myelitis

Diagnosis is aided by recognition of signs of systemic or ophthalmic disease, results of titres and CSF analysis. For viral infections, steroids may be temporarily palliative. Toxoplasmosis/neosporosis may be treated with clindamycin and trimethoprim/sulfadiazine (see below).

Trauma

Trauma, with or without vertebral body fracture or dislocation, may result in clinical signs of spinal cord dysfunction. Plain radiography may be performed as an initial diagnostic step but extreme caution must be used if vertebral instability is suspected. Patients should be strapped to a rigid board during the initial investigation, to prevent excessive movement and worsening of spinal cord trauma. Sedation may be required if the patient struggles against the strapping. If possible, imaging should be performed with the animal conscious in order to maintain normal muscle tone and limit movement of the spinal column. Myelography, MRI or CT may then be considered in order fully to characterize fractures, luxations or other spinal cord injury and to rule out complete spinal cord transection, which carries a hopeless prognosis.

Treatment options involve pain control and cage rest or surgical decompression and/or stabilization if marked spinal cord compression or vertebral column instability is present. An external splint applied from the scapulae to the base of the tail may be used to limit motion of the spinal column in cases of vertebral body fracture.

The use of corticosteroids in spinal cord injury remains controversial. The benefit of steroids comes primarily from free radical scavenging properties but also the anti-inflammatory effects and maintenance of blood flow to the spinal cord (Platt *et al*., 2005). In the 1980s, a protocol was developed using methylprednisolone sodium succinate that, when given within 8 hours of the onset of signs (30 mg/kg i.v; then 15 mg/kg at 2 and 6 hours; then 2.5 mg/kg/h for 24–48 hours), was shown to improve functional outcomes, both motor and sensory, in human patients (Bracken *et al*., 1984, 1990). After 8 hours, the treatment was associated with an increase in complications including aspiration pneumonia and risk of infection. Further studies have shown that treatment with methylprednisone in humans is associated with higher mortality and risk of infection in the face of only modest benefit (Short *et al*., 2000).

There is a lack of data in veterinary medicine to make clear recommendations for use of high-dose steroids in spinal cord injury.

Fibrocartilaginous emboli and acute non-compressive disc extrusion

Signs in dogs commonly begin during a period of exercise; mild transient pain may be noted. Signs may progress over the first 12 hours and then stabilize. Hemiparesis/paralysis may occur.

MRI is the imaging modality of choice in these patients. Changes include a focal hyperintensity on T2-weighted images with isointense lesions on T1-weighted images. There is little to no contrast enhancement. Differentiating between an ischaemic myelopathy and a non-compressive disc extrusion often requires histopathology.

As described above, the use of corticosteroids in spinal cord injury is controversial and remains as such in these cases. Initial work supported the use of steroids using various protocols, including high-dose therapy, for fibrocartilaginous emboli (Dyce and Houlton, 1993). However, further study has found no benefit for steroid use in ischaemic myleopathy in dogs (Nakamoto *et al*., 2009). Supportive care and physiotherapy should be provided.

Physio/hydrotherapy have been anecdotally associated with improved outcome. Severity of signs and prognosis vary with the extent and location of the cord infarct or damage. Infarcts occurring within either the cervicothoracic or lumbosacral intumescences carry a more guarded prognosis. One study of ischaemic myelopathy determined that a lesion to vertebral length ratio >2, or a lesion in >67% of the cross-sectional area of the spinal cord, was associated with an unsuccessful outcome (De Risio *et al*., 2008). Recovery may take months and may be incomplete.

Tetraparesis and paralysis

Tetraparesis and paralysis may result from peripheral nerve/muscle, cervical spinal cord and/or brainstem disease. Differentiating peripheral nerve and muscle disease from spinal cord and brainstem disease is essential for making the correct diagnosis. Disorders of the cervical spinal cord typically result in spasticity and exaggerated segmental reflexes. Disorders of peripheral nerve/muscle result in flaccidity, diminished segmental reflexes and rapidly progressing muscle atrophy (1–2 weeks).

Cervical cord and/or brainstem disease caudal to the thalamus

For discussions of intervertebral disc disease, neoplasia, discospondylitis, myelitis, trauma and fibrocartilaginous emboli, see Pelvic limb paresis and paralysis, above.

Atlantoaxial subluxation

Neck pain and signs attributable to disease of cervical spinal cord segments 1–5 may occur in young small-breed dogs. Flexing the neck may result in pain, worsening of clinical signs and respiratory paralysis. Survey radiographs may reveal subluxation of the first and second cervical vertebrae (increased space between the dorsal arch of C1 and the ventral aspect of the dorsal spinous process of C2) and possible abnormalities of the dens (Figure 9.4). If possible, radiographs should be performed without general anaesthesia, to prevent loss of muscle tone that prevents excessive flexion and worsening of compression. Cage rest, corticosteroid therapy and external fixation with a neck brace may result in improvement. An evaluation of 19 dogs with acute-onset clinical signs showed that medical management is a viable option, regardless of the severity of deficits on initial examination (Havig *et al*., 2005). Surgical stabilization may ultimately be required.



9.4 Lateral radiograph taken in neutral position demonstrating the typical findings of an atlanto-axial subluxation. There is increased space between the dorsal aspect of the atlas and the spinous process of the axis, as well as the dorsal displacement of the ventral axis from the ventral floor of the atlas.

Caudal cervical spondylomyelopathy ('wobblers')

This condition is most frequently seen in young Great Danes and in middle-aged Dobermanns. Signs of disease attributable to cervical spinal cord segment 6 to thoracic spinal cord segment 2 are most common, and often more than one site is affected. Cord compression and instability are confirmed with MRI, although flexed, extended and traction views can be obtained using CT, with or without myelography. The current opinion is that MRI is the modality of choice (De Decker *et al*., 2013). In the emergency situation, these animals may be treated in a manner similar to animals with intervertebral disc disease. Without surgery, many dogs will eventually show a progression of clinical signs. However, a retrospective comparison of both medical and surgical treatment in 106 dogs showed that outcome was not significantly different between groups and that median survival times were also similar at 36 months (da Costa *et al*., 2008).

Meningoencephalitis of unknown aetiology

Granulomatous meningoencephalitis and necrotizing encephalitis are considered to be due to immune system responses in the central nervous system. Clinical signs are typically acute in nature, progressive and have a multifocal or diffuse localization. Collectively, they can be considered meningoencephalitis of unknown aetiology, as they are treated much the same way. MRI may show multifocal hyperintense lesions on T2 and FLAIR image sequences. These lesions may or may not contrast enhance. CSF analysis may show increases in protein, mononuclear cells and non-degenerate neutrophils.

Definitive diagnosis requires biopsy. Prednisolone at immunosuppressive doses (1–2 mg/kg q12h for 5 days; then 1 mg/kg q24h for 3–6 weeks; then 0.5 mg/kg q24h for 3 weeks; then 0.5 mg/kg indefinitely) may result in initial improvement in neurological signs. Other agents have also been used in combination with corticosteroids, including cytosine arabinoside (administered at 200 mg/m^2 in four subcutaneous injections over a 24-hour period) or ciclosporin (administered at 3–6 mg/kg q12h). Other medications in use include: lomustine, mycophenolate mofetil, leflunomide and procarbazine. Prognosis is guarded and further evaluation of survival times is necessary; however, there are reports of up to 1025 day survival times with combination therapies (Talarico and Schatzberg, 2010).

Steroid-responsive meningitis

Signs of severe neck pain, fever, lethargy and neurological deficits attributable to disease of cervical spinal cord segments 1–5 may occur in young dogs. CSF analysis reveals marked increases in protein and in white blood cells, with non-degenerate neutrophils the most common cell type. Culture of the CSF is negative. Some dogs are afflicted by a more chronic form with a mononuclear pleocytosis present in CSF. Elevated serum and CSF IgA concentrations may help in diagnosis. The disease is considered an immune-mediated disorder. Treatment with glucocorticoids (prednisolone 1–2 mg/kg q12h for 3 days and then decreased over time to the dose necessary to control signs) is required for several months; relapse of clinical signs is common. C-reactive protein serum concentrations may be used to monitor response to therapy (Tipold and Schatzberg, 2010).

Causes and management of diseases of peripheral nerve, muscle and neuromuscular junction

Diseases of peripheral nerves and muscles commonly result in flaccid paresis or paralysis. Clinical signs include a short-strided gait, postural reaction deficits and diminished segmental reflexes. Postural reaction deficits may improve when the weight of the animal is lifted during testing. Neurogenic muscle atrophy is common.

Botulism

Signs of flaccid paralysis and hyporeflexia occur in dogs hours to days after ingesting preformed toxin. Cranial nerve deficits include decreased ability:

- To blink the eyelids
- To lift the upper lip
- To close the mouth
- To lap water or swallow.

Change in voice, regurgitation, megaoesophagus, decreased perineal reflex, faecal and urinary incontinence, and respiratory paralysis may occur. Botulism is suspected from the history, clinical signs and electrodiagnostic testing (decreased compound motor action potential following nerve stimulation). Toxin may be identified in food, serum, stomach contents or faeces early in the course of the disease. Supportive care is given, a gastrostomy tube is placed if needed and the animal is monitored for aspiration pneumonia and respiratory paralysis. Signs may resolve with supportive care within 2–3 weeks.

Acute polyradiculoneuritis and polyneuritis

Affected dogs may have been recently vaccinated or have a history of exposure to raccoons; some dogs may have no history of exposure to either. A similar syndrome has been seen in cats, and in humans this condition is

known as Guillain–Barré. Flaccid paralysis and hyporeflexia occur. Facial muscle paresis and a change in voice are common. Respiratory paralysis may occur. Interestingly, however, tail and neck motion, swallowing, and faecal and urinary continence are often maintained. The animal may be hyperaesthetic to touch. CSF analysis may show an increase in protein and cells. Electromyography may reveal fibrillation potentials and positive sharp waves in the majority of muscles tested. Nerve conduction velocity is slow, and evoked potentials may be decreased in amplitude. Biopsy specimens of nerve root or nerve may show inflammatory cell infiltrates, demyelination and axonal loss. Prednisolone (1 mg/kg q12h for 1–2 weeks; then 1 mg/kg q24h for 1 month) may be given; however, there is controversy as to whether it has any effect on the progression of this disease. Supportive care to prevent and treat decubital ulcers and urinary tract infections and observation for respiratory muscle paresis should be performed.

One study found that dogs given human intravenous immunoglobulin recovered to ambulation at a median of 27.5 days compared with 75.5 days without therapy. There were adverse reactions including anaphylaxis and haematuria. This result was not statistically significant and larger patient numbers are necessary (Hirschvogel *et al*., 2012). Recovery may take 6–8 weeks and may be incomplete. Signs may recur.

Tick paralysis

Some species of tick can cause signs of peripheral neuromuscular disease that start to develop several days following attachment of the tick. This disease is reported in the USA and a more severe form occurs in Australia. In the USA, *Dermacentor variabilis* and *D. andersoni* (the Rocky Mountain wood tick) are incriminated most often. Other species that occasionally cause paralysis are *Ixodes cornuatus* and *I. hirsti. Ixodes scapularis*, the principal vector of the agent of Lyme disease (*Borrelia burgdorferi*) in the northeast, midwest and southeast of the USA, can also cause tick paralysis in dogs. *Ixodes pacificus* has been incriminated in dogs in the Grass Valley area (Nevada County) of northern California. In Australia, especially along the east coast, *Ixodes holocyclus* is the most important species.

Affected dogs typically still have the tick attached. Flaccid paralysis and hyporeflexia occur. Nystagmus, change in voice, dysphagia, weakness of facial muscles and masticatory muscles, and respiratory paralysis may occur. Electrodiagnostic testing may show reduction in amplitude or absence of the compound motor action potential following nerve stimulation and a slow nerve conduction velocity. Removal of ticks results in resolution of clinical signs within 24–72 hours. Ticks may be hard to find, however, and whole-body shaving may be necessary. Application of tick bathing products or spot-on treatment may prove helpful.

Insulin-secreting tumours

Serum glucose concentrations <2.8 mmol/l may result in clinical signs. Flaccid paralysis, hyporeflexia, lethargy, bradycardia, muscle tremors, hypothermia, disorientation and seizures may occur. Electromyographic examination may show fibrillation potentials, positive sharp waves and complex repetitive discharges. Small quantities of food high in protein, fat and complex carbohydrates may be provided frequently. Diazoxide (10 mg/kg q12h) and prednisolone (0.5 mg/kg/day) may be given.

Tetanus

Tetanus is the continuous tonic contraction of a muscle due to rapidly repeated stimulation. The causative organism, *Clostridium tetani*, synthesizes a potent neurotoxin (tetanospasmin) following germination of spores under anaerobic conditions, typically after infecting a deep wound. The toxin then travels in a retrograde fashion along axons within a peripheral nerve into the central nervous system. Clinical signs occur due to the ability of the toxin to inhibit the release of neurotransmitters (glycine and GABA) from upper motor neurons and interneurons of the brainstem and spinal cord, resulting in a release of the lower motor neuron from inhibition. Clinical signs of generalized tetanus include extensor rigidity of appendicular muscles, risus sardonicus and trismus. Dyspnoea, dysphagia, and urinary and faecal retention may occur. Focal tetanus occurs when rigid extension is limited to one limb or muscle group.

Treatment with penicillin G (20,000–100,000 IU/kg i.v. q6h) is recommended and, if a wound is identified, it should be debrided to remove *C. tetani*. Tetanus antitoxin is given at 100–1,000 IU/kg i.v. A small test dose may be given initially to observe for an anaphylactic reaction. The patient should be kept in a quiet environment with little stimulation. Diazepam and acepromazine may be given to relax or calm the patient. Methocarbamol may be given to help with muscle relaxation (55–100 mg/kg i.v. q30–60 minutes up to 330 mg/kg/day). Nursing care is essential to maintain hydration and nutrition until the patient is able to drink and eat without assistance. If paralysis of the intercostal muscles occurs, ventilatory support may be necessary, although this is uncommon.

A study of 20 dogs with tetanus found that mostly young, large-breed dogs were affected. Twelve of these dogs had a source of infection identified. There was no adverse reaction in the 16 dogs that received the antitoxin. The mortality rate was 50% and the time to recovery in the surviving dogs was about 1 month (Bandt *et al*., 2007). A separate study of 38 dogs and risk factors identified younger dogs at greater risk for developing more severe signs. Dogs that had abnormal heart rate or blood pressures had a worse prognosis (Burkitt *et al*., 2007).

Toxoplasmosis/neosporosis

In puppies, flaccid paralysis that progresses to rigid extension of the pelvic limbs occurs to such a degree that the joints are no longer able to flex, even under general anaesthesia. Evidence of systemic disease may be recognized. Increased antibody titres occur. Trimethoprim/sulfadiazine (15 mg/kg q12h for 2 weeks) and clindamycin (10 mg/kg q12h for 8 weeks) may result in improvement of clinical signs; however, once hindlimb rigidity has developed, improvement will not occur with therapy. If only one limb is affected, amputation may be considered in these animals.

Aortic thromboembolism

Animals are in pain, limbs are cool, pulses are weak or absent and muscles are firm. Abdominal ultrasonography may identify a thrombus in the aorta. Analgesics, intravenous fluids, heparin, acepromazine and aspirin may be given (see Chapter 6 for more details). Thromboembolism has been associated with cardiomyopathy in cats and with protein-losing nephropathy in dogs (Flanders, 1986; Van Winkle *et al*., 1993).

Others

Hypoadrenocorticism and diabetes mellitus may cause hindlimb paresis in addition to signs of metabolic disease. Diabetic cats and dogs may have a plantigrade stance. Control of metabolic disease commonly results in resolution of neurological dysfunction. Early polyneuropathy or myasthenia gravis may result in signs of hindlimb paresis (see Episodic weakness/syncope).

Episodic weakness/syncope

Episodic weakness and collapse may occur due to neuromuscular or brain disease, syncope or metabolic disorders.

Neuromuscular disorders

Acquired myasthenia gravis

At least three clinical presentations may occur (Dewey *et al*., 1997):

- **Focal myasthenia gravis:** animals exhibit facial, pharyngeal and/or laryngeal muscle dysfunction without appendicular muscle involvement. Megaoesophagus, regurgitation and aspiration pneumonia may occur
- **Generalized myasthenia gravis:** animals exhibit appendicular muscle weakness with a stiff, short-strided gait, with or without signs of facial, pharyngeal and/or laryngeal muscle dysfunction. Strength may or may not return following periods of rest
- **Acute fulminating myasthenia gravis:** signs include a sudden, rapid progression of severe appendicular muscle weakness, resulting in recumbency which is unabated by rest; frequent regurgitation associated with megaoesophagus; respiratory difficulty; and facial, pharyngeal and/or laryngeal muscle dysfunction.

For diagnosis, blood acetylcholine receptor antibody concentrations may be elevated (>0.6 nmol/l in dogs and >0.3 nmol/l in cats). Edrophonium (0.1–0.2 mg/kg i.v.) may result in dramatic improvement in gait for 1–2 minutes. Pretreatment with atropine (0.02 mg/kg i.v.) is recommended when performing an edrophonium test to reduce the risk of serious cardiovascular side effects.

Compound action potentials recorded from the interosseous muscle may show a 10% or greater decremental response following repetitive stimulation (Hopkins, 1992).

Emergency management of suspected myasthenia is largely supportive, with attention focused on respiration, care of the recumbent patient, treatment of aspiration pneumonia and management of nutrition while awaiting antibody test results. Long-term management includes administration of oral pyridostigmine (0.2–2.0 mg/kg q8–12h); alternatively, in animals with significant dysphagia and regurgitation, neostigmine can be given intramuscularly (0.04 mg/kg q6–8h). Animals should be kept warm and exercise restricted. Animals with dysphagia and megaoesophagus should be fed from a height with the head and neck elevated for 10 minutes after eating. Aminoglycoside antibiotics should be avoided due to the possibility that they may exacerbate neuromuscular blockade.

Prednisolone may result in a rapid worsening of clinical signs and its use is contraindicated in the presence of aspiration pneumonia. However, in the authors' experience, prednisolone may improve pharyngeal dysfunction sooner than cholinesterase inhibitors alone. A starting dose of 0.5 mg/kg/day increased to 2 mg/kg/day over 1 week has been suggested when aspiration pneumonia is not present (Le Couteur, 1988). Additionally, treatment with azathioprine has proven useful and may minimize side effects due to steroid administration. Five dogs were treated with azathioprine at 2 mg/kg along with pyridostigmine and four of these had an 81% reduction in antibody concentration that coincided with clinical improvement (Dewey *et al*., 1999). Although single reports of successful treatment have been found, a study of 15 dogs receiving combination therapy with mycophenolate mofetil showed no benefit over treatment with pyridostigmine alone (Dewey *et al*., 2010).

Exertional rhabdomyolysis

Racing Greyhounds may present with scuffing of the nails of the hindlimbs, muscle pain, tachypnoea, collapse and hyperthermia within 72 hours of exercise. Increased creatine kinase, lactate dehydrogenase, aspartate aminotransferase, blood lactate and myoglobin may occur. Renal failure may also occur. Treatment consists of intravenous fluids (to treat shock and to aid in the excretion of myoglobin), cold water baths and pain medication. Intravenous bicarbonate may be used to support cardiovascular and renal function. Alkalinization of the urine may also inhibit the formation of haematin in acidic urine, which can have toxic effects (Porzio *et al*., 1997).

Exercise-induced collapse

Some Labrador, Chesapeake Bay and Curly Coated Retrievers, Boykin Spaniels and Pembroke Welsh Corgis have been found to carry a mutation in the dynamin-1 gene (*DNM1*). This encodes for enzymes that participate in cellular endocytosis (i.e. synaptic vesicles). In Labrador Retrievers homozygous for the mutation, a syndrome of collapse occurs following 5–20 minutes of intense exercise. It begins with hindlimb incoordination and progresses to a non-painful flaccid paraparesis, which can involve the thoracic limbs as well. Loss of the patellar reflex is common. Hyperthermia is also noted. Dogs recover after 15–30 minutes of rest, but deaths have been reported. There is no effective treatment, and dogs should be restricted to mild to moderate exercise (Minor *et al*., 2011).

Polymyositis

Dogs and cats of any age may present with generalized weakness that worsens with exercise (Evans *et al*., 2004). The gait is stiff and short-strided, and dysphagia, regurgitation, megaoesophagus, change in voice, painful appendicular muscles, fever and lethargy may occur. Increases in creatine kinase, aspartate aminotransferase, lactate dehydrogenase and antinuclear antibody may occur. Electromyography may reveal fibrillation potentials, positive sharp waves and bizarre high-frequency discharges. Muscle biopsy reveals lymphoplasmacytic inflammation and muscle necrosis. Toxoplasmosis and neosporosis should be ruled out with titres and muscle biopsy. Prednisolone may be given (1 mg/kg q12h initially) and reduced to the lowest dose necessary to control signs. Pharyngeal and oesophageal muscle involvement may result in aspiration pneumonia.

Masticatory myositis, an autoimmune condition with antibodies directed at the 2M muscle fibres found in the masticatory musculature of dogs, may present with swelling

and pain around the head. Specific 2M antibody titres or biopsy samples of the temporalis or masseter muscles can be evaluated for diagnosis.

Extraocular myositis is a similar auto immune condition with marked swelling of the extraocular muscles causing severe bilateral exophthalmos. Diagnosis from clinical signs alone or with MRI is generally sufficient. Treatment for both masticatory and extraocular myositis is largely the same as described above.

Brain disease

Narcolepsy/cataplexy

Episodes last seconds to minutes and are marked by acute collapse, decreased muscle tone and rapid eye movement sleep. Episodes may be provoked by excitement, food or physostigmine (0.025–0.1 mg/kg i.v.). Minimizing excitement and giving imipramine hydrochloride (0.5–1 mg/kg orally q8h) or venlafazine (2.5 mg/kg/day) may decrease the number of events.

Syncope

Syncope due to cardiovascular or respiratory disease occurs most commonly during periods of exercise or excitement.

Cardiovascular disease

Episodic weakness, ataxia, lethargy, dyspnoea and syncope may occur. Evidence of a heart murmur, irregular heart rate or rhythm, bradycardia or tachycardia, weak or irregular pulses, polycythaemia, heartworm infection and electrocardiographic abnormalities between or during events suggest cardiovascular disease as the cause. More details can be found in Chapter 6.

Respiratory disease

Hypoxia, particularly if chronic, may result in syncope.

Metabolic disorders

Hyperthyroidism

Episodic weakness, decreased ability to jump, muscle tremors and ventroflexion of the neck may occur in addition to other signs of hyperthyroidism (Joseph and Peterson, 1992). Post-insertional trains of positive sharp waves are reported on electromyographic examination. Stress should be decreased and methimazole administered (10–15 mg/day orally divided q12h).

Hypoadrenocorticism

Episodic weakness, stiff, stilted hindlimb gait, muscle tremors, vomiting, anorexia, weight loss, dehydration, weak pulses and shock may occur. Intestinal parasites (whipworms in particular) may cause clinical signs mimicking those of an Addisonian crisis. Stress should be decreased, intravenous fluid support provided and hypoglycaemia treated. Dexamethasone sodium phosphate (0.1–0.2 mg/kg i.v.) may be given until the diagnosis is confirmed (see Chapter 16).

Hyperkalaemia

Appendicular and neck muscle weakness, bradycardia, dysrhythmias, weak pulses, electrocardiographic abnormalities and hyporeflexia may occur when serum potassium is >6.5 mmol/l. Weakness resolves with treatment of hyperkalaemia.

Hypokalaemic myopathy

This is seen principally in cats. Ventroflexion of the neck, a stiff, short-strided gait, episodic weakness, pain on muscle palpation and respiratory muscle paresis/paralysis may occur. A serum potassium level <3.5 mmol/l, increased creatine kinase, azotaemia and metabolic acidosis may be found. Electromyographic examination may reveal fibrillation potentials and positive sharp waves. Mildly or moderately affected cats may be treated with oral potassium supplementation (5–8 mmol potassium q12–24h). Intravenous potassium infusion (CRI <0.5 mmol/kg/h) may be given to those with severe weakness and respiratory depression. Occasionally, hypomagnesaemia may accompany hypokalaemia and exacerbate the weakness. Weakness resolves with treatment of hypokalaemia and, if present, hypomagnesaemia.

Others

Other diseases that may present with episodic weakness include Episodic Falling Syndrome of Cavalier King Charles Spaniels, mitochondrial myopathy of Clumber and Sussex Spaniels and Old English Sheepdogs, phosphofructokinase deficiency of English Springer Spaniels, panosteitis, hypertrophic osteodystrophy, polyarthritis, anaphylactic reactions, and the presence of a phaeochromocytoma. A good history is necessary to rule out epileptic activity as a cause for paroxysmal collapse.

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Chapter 10

Ophthalmological emergencies

Cristina Seruca and Debbie Mandell

Ocular emergencies can be intimidating and frustrating for veterinary surgeons (veterinarians). While the majority of general practitioners do not have the most advanced equipment to perform ophthalmic examinations or surgery (e.g. slit lamps, operating microscopes), many ophthalmological emergencies can be diagnosed and treated successfully with the basic equipment available to every veterinary surgeon.

Many animals present to the practice because of signs of ocular pain (blepharospam, tearing, photophobia), changes in appearance of the eye (colour, pupil), or reduced vision or blindness. It is important to acquire a thorough medical history, general physical examination and perform a complete bilateral ophthalmic examination in every animal that presents for an ocular emergency. This examination should include distant observation (assessment of globe size and head symmetry); a neuro-ophthalmic examination, including assessment of the menace response, dazzle reflex, pupillary light reflexes (PLRs) (both direct and indirect) and palpebral reflex; and a detailed examination of all ocular structures, including the eyelids, conjunctiva, nictitating membrane, nasolacrimal system, cornea, anterior chamber, iris, lens and the posterior segment, including the vitreous and fundus. A Schirmer tear test (STT) should be performed before any topical medications are placed in the eye. The intraocular pressure (IOP) should be measured with appropriate equipment, when available. The fluorescein test should be performed in red or painful eyes, in eyes with corneal irregularity or corneal discharge, and history of ocular trauma. In exceptionally painful eyes, topical anaesthesia may be needed to facilitate an ophthalmic examination. Complementary diagnostic procedures (e.g. ocular ultrasonography, electroretinography, laboratory work-up) may be indicated in some cases.

This chapter discusses the diagnosis, treatment and prognosis of common ophthalmological emergencies. When a definitive ophthalmic diagnosis cannot be achieved, when the disease is not responding to treatment, when there are conflicting disease processes in the same eye, or when advanced surgical techniques are indicated, an ophthalmologist should always be consulted.

Proptosis

Definition and causes

Proptosis is an acute forward displacement of the globe with simultaneous entrapment of the eyelids behind the equator (Gilger *et al*., 1995). It can occur secondary to any blunt trauma to the head, such as being hit by a car, or bite wounds (Figure 10.1). Brachycephalic breeds are predisposed because they have shallow orbits and a relatively large eyelid fissure.



10.1 (a) Proptosis of the left globe in a French Bulldog puppy. There is entrapment of the eyelids as well as severe swelling and hyperaemia of the bulbar conjunctiva. Note no extraocular muscles have been torn. On examination, the patient had positive direct and indirect PLRs of the left eye. The eye was replaced and a temporary tarsorraphy was performed. (b) Severe proptosis of the left globe (lateral view) with avulsion of several extraocular muscles in a cross-breed dog. In spite of the clear and intact anterior segment, the eye was enucleated because of the poor prognosis.
(a, Courtesy H Appelboam; b, Courtesy of N Escanilla)

Clinical signs and management

Proptosis of the globe is a true ophthalmic emergency which requires rapid assessment and immediate medical and surgical treatment. Even when vision cannot be preserved, early and adequate treatment may allow the globe to be salvaged.

Clinical signs and management depend on the cause of the proptosis and the degree of damage to the globe and extraocular structures. A detailed examination of the different anatomical structures of the globe should be performed to determine the prognosis for vision and functionality of the globe, and decide on the appropriate treatment. As the menace response cannot usually be assessed, evaluation of the direct and consensual PLRs may provide some information regarding the integrity of the posterior segment. Eyes that have direct or indirect PLRs on initial examination have a better prognosis. The amount of

extraocular muscle damage also provides information regarding the prognosis. If more than two ocular muscles are avulsed, the vascular supply and innervation to the globe is compromised, therefore the globe should be enucleated. Scleral ruptures are usually associated with intraocular haemorrhage and loss of shape and turgor of the globe. In these cases, enucleation should be recommended. If there is marked hyphaema, especially if combined with avulsion of more than one extraocular muscle, prognosis is guarded and enucleation may be considered.

Replacement of the globe followed by a temporary tarsorrhaphy should be attempted if the eye and extraocular muscles are relatively undamaged and fewer than two extraocular muscles have ruptured. If there is any doubt as to whether the eye can be saved, it is often preferable to try to salvage the globe rather than remove it.

The owner should be warned that replacing the globe might be only for cosmetic reasons; return of vision cannot be guaranteed.

Replacement and temporary tarsorrhaphy

Although the eye should be replaced as soon as possible, if the animal has sustained significant head trauma anaesthesia should be postponed until its condition is stable. While stabilizing the animal, topical lubricants or ophthalmic antibiotic ointments should be applied to the globe to protect the cornea and prevent desiccation.

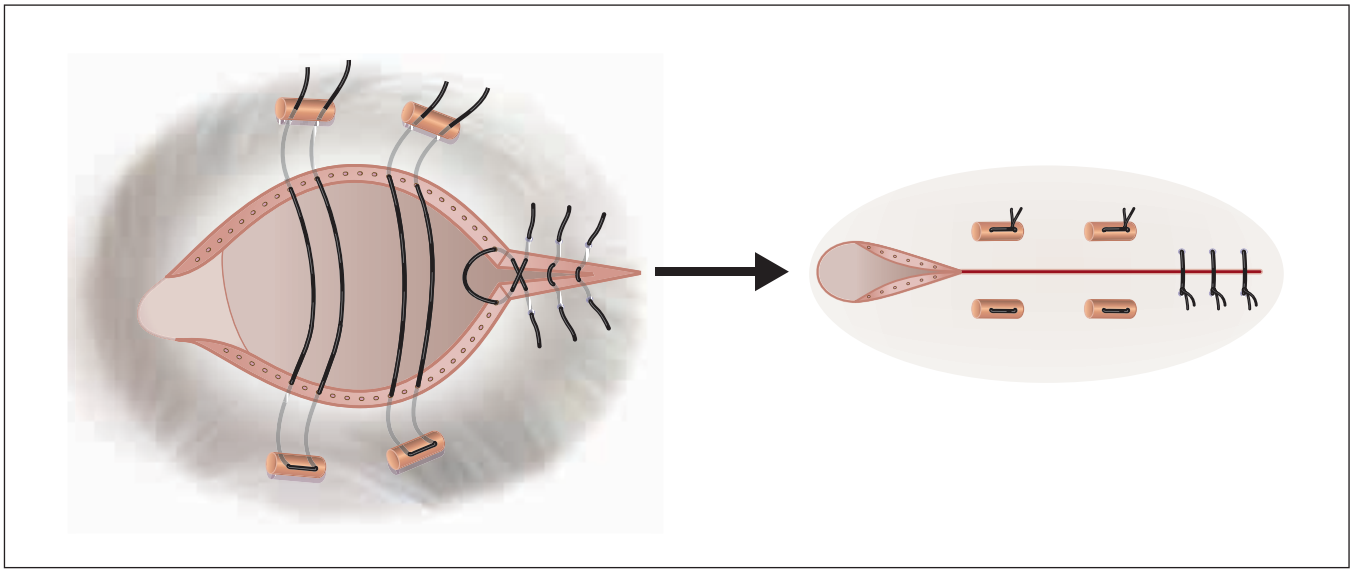
Once the animal is anaesthetised, the globe is cleansed with sterile saline or lactated Ringer's solution. The eyelids should be gently engaged using strabismus hooks or Allis forceps and pulled both up and away from the globe. A lateral canthotomy may be necessary to facilitate replacement of the globe. While lifting the eyelids out and up, gentle pressure is placed on the eye to replace it into the orbit. A wet cotton ball or wet gauze can be used to apply pressure evenly.

Orbital haemorrhage and tissue swelling may result in some degree of exophthalmia after globe replacement; therefore, a temporary tarsorrhaphy must be performed to prevent recurrence. Two or three horizontal mattress sutures are then placed (Figure 10.2); 0.7 or 1.5 metric (6/0 or 4/0 USP) nylon can be used with pieces of a 3.5 or 5 French red rubber catheter, intravenous or butterfly catheter tubing as rubber stents to prevent the suture from cutting into the skin. All sutures should be preplaced before tying. The suture should go through the stent, enter the lid 6–8 mm from the upper lid margin, exit through the orifices of the meibomian glands, then enter through the orifices of the lower lid meibomian glands, exit 6–8 mm from the lower lid margin and go through a second stent (see Figure 10.2). The needle then goes back in the reverse direction and the suture is tied at the dorsal aspect. Sutures placed too far from the lid margin can cause entropion. Sutures placed through the conjunctiva may result in an 'egg slicing' effect and damage to the cornea. If a lateral canthotomy was previously performed, it can be closed by a figure-of-eight suture at the lid margin and further simple interrupted sutures with 0.7 or 1.0 metric (6/0 or 5/0 USP) nylon, polyglactin 910 (Vicryl) or poliglecaprone (Monocryl). A small space should be left open medially to allow placement of medications.

Aftercare

Aftercare consists of broad-spectrum topical antibiotics (e.g. triple antibiotic (neomycin and polymyxin B along with bacitracin or gramicidin), chloramphenicol, or oxytetracycline every 6–8h). Oral broad-spectrum antibiotics (e.g. co-amoxiclav; cefalexin) should also be used for 2 weeks. Anti-inflammatory doses of systemic corticosteroids at a tapering dose over 1–2 weeks will decrease further damage to the optic nerve, periorbital swelling and intraocular inflammation. An Elizabethan collar must be worn at all times.

Frequent re-evaluations should be performed to make sure that the client is able to administer medications, the sutures are not abrading the cornea, the animal is not febrile and that there is no discharge crusted over the eye. The sutures are removed after 7–15 days starting medially, to protect the globe until swelling completely subsides.



10.2 Temporary tarsorrhapy. The lid fissure is closed by two or three U-shaped sutures. Rubber pieces, for example infusion or butterfly catheter tubing, are used to prevent the suture from cutting into the skin. All sutures should be preplaced before tying. The margins of the upper and lower lid should be perfectly apposed in order to avoid a rubbing effect of the sutures on the cornea. A small space should be left open medially to allow placement of medications. If previously performed, the lateral canthotomy can be closed by a figure-of-eight suture at the lid margin and further simple interrupted sutures.

Complications with replacement

Complications following replacement of the eye into the orbit include blindness, strabismus, sensory deficit of the cornea, keratoconjuncitivits sicca (KCS), exposure keratitis, glaucoma, cataract, lens luxation and phthisis bulbi, which is defined as a small, shrunken and deranged globe due to massive or chronic inflammation. Lateral or dorsolateral strabismus is a common sequel resulting from avulsion of the medial and ventral rectus muscle. Surgical repair of extraocular muscle tears may be indicated in select cases. The globe often returns to a near normal position over the course of several months. If the animal has lagophthalmos and exposure keratitis, a medial or lateral canthoplasty may help to protect the cornea. Owners must be warned that enucleation may still be necessary.

Prognosis

Due to the stretching of the optic nerve, the prognosis for vision is guarded (only 20% of proptosed globes regain some functional vision) but the prognosis for cosmetic repair is fair. A successful visual outcome is more likely if: the eye has vision on presentation; periocular tissue damage is minimal; direct or indirect PLR is present; proptosis is treated early; and the eye is evaluated frequently to circumvent complications. Brachycephalic breeds that require less force to proptose an eye have a better chance of regaining vision than dolichocephalic dogs or cats where a significant amount of force is necessary and more traumatic damage to the eye is likely to have occurred. Proptosis in cats is usually associated with a poor visual prognosis compared with dogs, since the feline optic nerve lacks the degree of sigmoid flexure present in dogs and therefore is more prone to injury when the globe is rostrally displaced.

Enucleation

An ophthalmology or surgery text should be consulted for enucleation procedures. Figure 10.3 shows the basic principles of enucleation.

Eyelid laceration

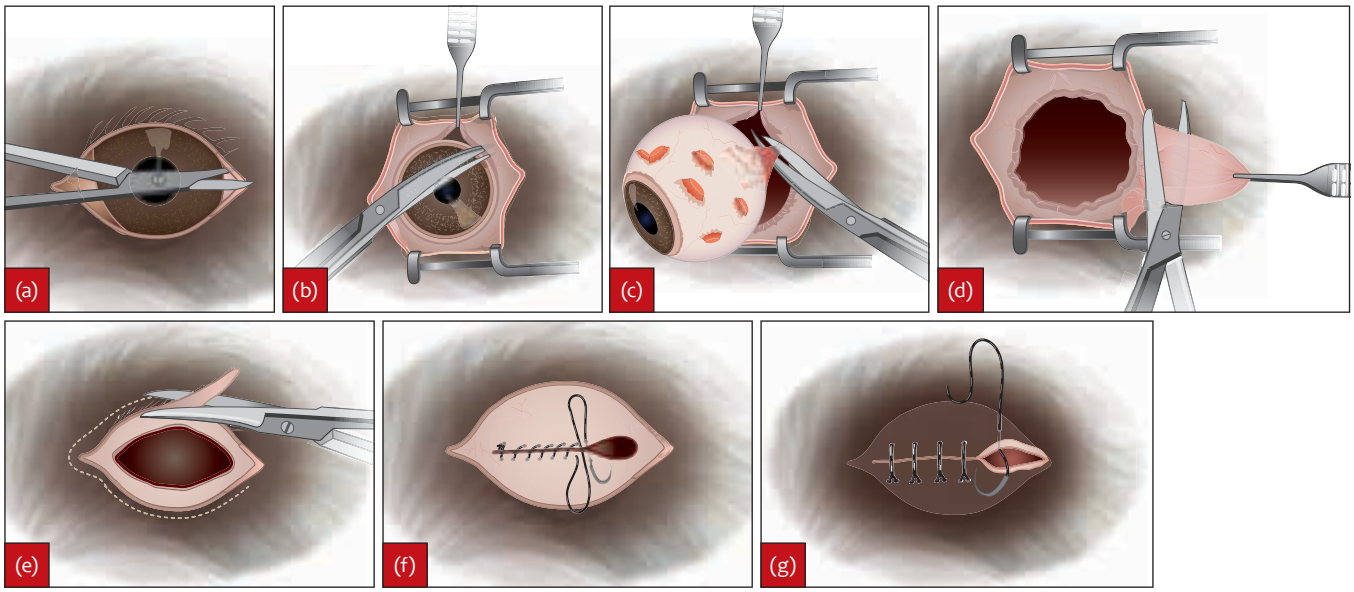
Definition and diagnosis

Traumatic eyelid lacerations are frequently seen in young dogs and cats and require surgical repair. Eyelid lacerations may be divided into partial and full-thickness, marginal (if the laceration crosses the lid margin) (Figure 10.4a) and non-marginal. They may also include the nasolacrimal system, usually the lacrimal puncta and canaliculi. Despite the severity of the eyelid laceration, a thorough ocular examination should be performed to identify and treat any associated ocular lesions, such as a corneal ulcer or uveitis.

Treatment

Eyelid lacerations should be repaired as soon as possible to avoid infection and reduce scarring and secondary corneal damage, thereby optimizing long-term outcome. The eyelids should be clipped gently and the wound in the lid margin and in the conjunctival sac must be thoroughly irrigated with a dilute (1:50) betadine solution. If the laceration affects the medial canthus or the medial third of the lower lid, the nasolacrimal puncta should be identified, cannulated and flushed to ensure patency.

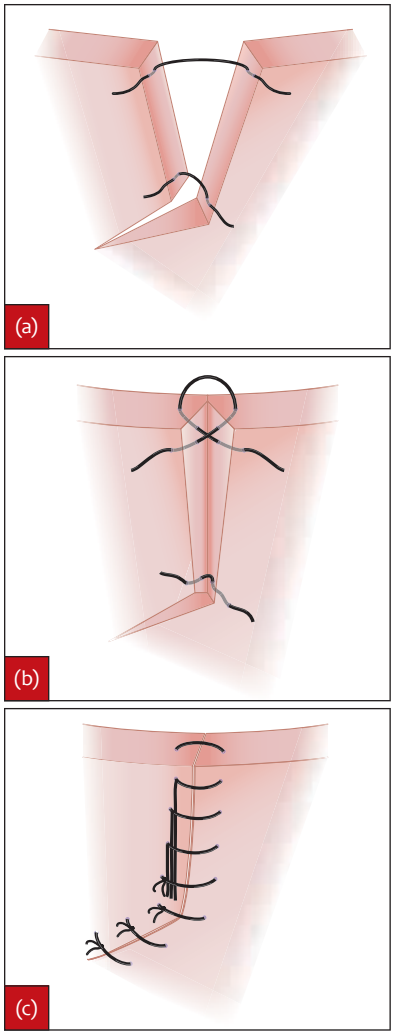
Tissue debridement must be minimal, since tissue resection may result in entropion/ectropion, decrease of the eyelid opening, or lid distortion. Loose parts (over



10.3 Subconjunctival enucleation. (a) A lateral canthotomy is performed. (b) The globe is dissected free from the conjunctiva and Tenon's capsule through a bulbar conjunctival incision made approximately 5 mm posterior to the limbus. (c) The extraocular muscle insertions are dissected from the globe and the optic nerve is transected. There is no need to clamp the optic nerve with haemostatic forceps prior to transecting it. Traction on the optic nerve must be avoided in order not to damage contralateral optic nerve fibres at the crossover point in the optic chiasm. (d) The cavity is packed with gauze sponges for temporary haemostasis, and the nictitating membrane and all remaining conjunctiva are completely removed. (e) A 3–5 mm section of the eyelid margin is removed with scissors. (f) The gauze sponges are removed and the orbital fascia and periorbita are sutured with 1.5 metric (4/0 USP) absorbable suture material in a simple continuous or interrupted pattern. Some ophthalmologists implant an appropriately sized silicon prosthesis in the orbit prior to closing the orbital fascia and periorbita. (g) The skin is closed with simple interrupted sutures using 1.0 or 1.5 metric (5/0 or 4/0 USP) non-absorbable monofilament suture material (e.g. nylon).



10.4 (a) Full-thickness marginal eyelid laceration in a 2-month-old Domestic Shorthair kitten. (b) Postoperative appearance of the same eye. The wound margins were minimally debrided and sutured in two layers as described in Figure 10.5. The ends of all skin sutures are left long and tucked under the subsequent suture to ensure they are directed away from the cornea.



10.5 Suturing a full-thickness marginal laceration. (a) The subcutaneous tissue is sutured using an absorbable 0.7–1.0 metric (6/0–5/0 USP) suture material (e.g. poliglecaprone 25, polyglactin 910). The lid margin and the angles of the wound are sutured first, followed by the remaining subcutaneous tissue. (b) The skin is closed with simple interrupted non-absorbable 0.7–1.0 metric (6/0–5/0 USP) monofilament sutures (e.g. nylon). The free lid margin should be apposed very precisely with a figure-of-eight suture. The angles of the wound are sutured afterwards, and then the remaining wound. (c) The ends of skin sutures that are close to the lid margin are left long and tucked under the subsequent suture to ensure they are directed away from the cornea.

1 mm), especially of the lid margin, should not be excised but used to fill the defect. If the wound margins need to be 'freshened', gentle scraping of tissue edges with a scalpel blade may be performed until bleeding is noted. If the lid margin is not involved, the skin can be sutured as a skin laceration, avoiding tension on the lid margins.

Full-thickness lacerations should be sutured in two layers, using an absorbable 0.7–1.0 metric (6/0–5/0 USP) suture material in the subcutaneous tissue and simple interrupted non-absorbable 0.7–1.0 metric (6/0–5/0 USP) monofilament sutures (e.g. nylon) in the skin. The subcutaneous sutures should not pass through the conjunctiva to avoid contact between the suture and the corneal surface. If the lid margin is involved, the margin should be apposed very precisely with a figure-of-eight suture. After the lid margin has been closed, the angles of the wound are brought together with simple, interrupted sutures and the remaining parts of the wound are then closed. The ends of the skin sutures positioned close to the lid margin should be left long and tucked under the subsequent suture (Figure 10.4b and 10.5) or be cut as short as possible to prevent irritation of the cornea. If there is significant loss of tissue (more than one-third of the length of the eyelid) requiring plastic surgical repair, or the wound involves the lower lacrimal puncta and/or canaliculi, the patient should be referred to a veterinary ophthalmologist since appropriate magnification and experience are required for correct surgical repair. Aftercare consists of the administration of systemic (e.g. cefalexin) and topical antibiotics and use of an Elizabethan collar to prevent self-trauma. Systemic non-steroidal anti-inflammatory drugs (NSAIDs) may also be administered to decrease tissue swelling and minimize pain.

Complications

Complications post repair including entropion/ectropion, trichiasis, lid distortion and corneal ulceration may occur if surgery was not performed promptly and accurately.

Prognosis

The prognosis is good to excellent if the eyelid margins can be promptly and successfully repositioned and minimal tissue is lost.

Conjunctivitis

Definition and causes

Conjunctivitis is inflammation of the conjunctiva. The most common causes are listed in Figure 10.6. In cats, conjunctivitis is most commonly due to an infection whereas in dogs it is most commonly due to allergic processes and tear deficiency.

Cats
• Lipogranulomatous conjunctivitis • Eosinophilic conjunctivitis Infection: • Viral (feline herpesvirus 1, calicivirus) • Bacterial (*Chlamydia* spp.,) • *Mycoplasma* • Parasitic
Dogs
• Allergic conjunctivitis • Follicular conjunctivitis • Contact hypersensitivity • Keratoconjunctivitis sicca • Eyelid abnormalities • Ligneous conjunctivitis Infection: • Viral (canine distemper virus, canine herpesvirus) • Fungal • Rickettsial • Parasitic • Protozoal (*Leishmania infantum*) • Bacterial

10.6 The most common causes of conjunctivitis.

Clinical signs

Clinical signs of conjunctivitis include blepharospasm, ocular discharge, conjunctival hyperaemia, chemosis (conjunctival oedema) and follicle formation.

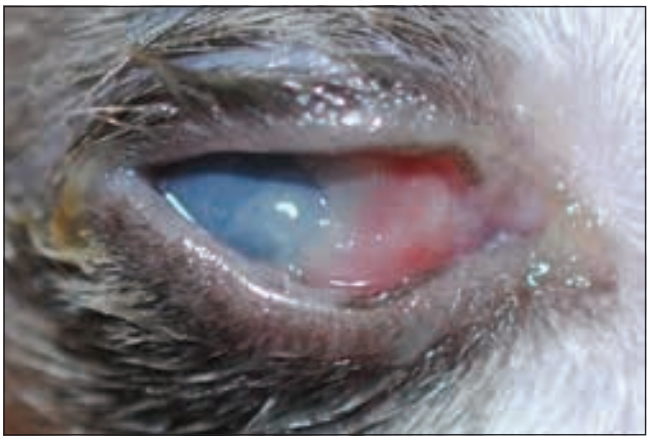
Diagnosis

It is very important to distinguish between conjunctivitis and 'a red eye'. Ocular redness, which can result from conjunctival hyperaemia or episcleral congestion, is a clinical sign that can occur with many ocular conditions, including corneal disease (such as corneal ulcers), uveitis, glaucoma, orbital disease, conjunctivitis and septic shock. As many ocular diseases can cause 'a red eye', a complete ophthalmic examination should always be performed when this clinical sign is present. Conjunctival hyperaemia should be differentiated from episcleral congestion, which can occur with glaucoma, uveitis and severe corneal disease. Generally, the conjunctival vessels are smaller in diameter, have a branching pattern, are mobile when moved with a cotton swab tip, and blanch quickly with the topical application of adrenaline (epinephrine). Episcleral vessels are larger in diameter, are not mobile and do not blanch quickly with the topical application of adrenaline.

The diagnosis of conjunctivitis is based on the clinical signs and ophthalmic examination.

Feline herpesvirus type 1 (FHV-1) is a major cause of conjunctivitis in both kittens and adult cats. Primary FHV-1 infection is usually accompanied by malaise and respiratory signs. In young cats, severe FHV-1 infection can cause large areas of ulceration of the conjunctival surface and sometimes of the corneal surface as well (Figure 10.7). These ulcerated areas will form adhesions (symblepharon) very quickly that may involve the entire ocular surface, resulting in blindness.

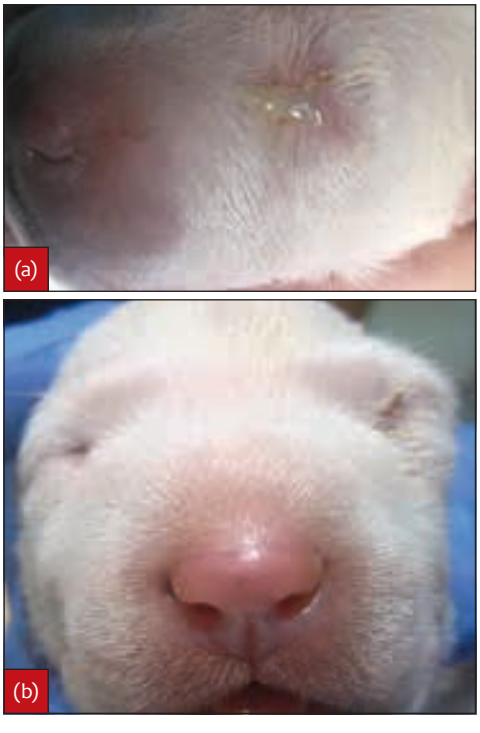
Chlamydia spp. is the second most common cause of conjunctivitis in cats. Chemosis is a prominent feature of *Chlamydia* infection. Mild respiratory signs may also be present in acute infections. With chronicity, membranous or follicular conjunctivitis can be noted.



10.7 Severe herpesvirus keratoconjunctivitis in a 2-month-old kitten. Note the purulent discharge, conjunctival hyperaemia, diffuse corneal oedema and corneal ulceration. The nictitating membrane is elevated and immovable due to symblepharon.

Polymerase chain reaction (PCR) is now the mainstay diagnostic technique for FHV-1, *Chlamydia* spp., *Mycoplasma* spp. and calicivirus. However, studies have found that samples from the conjunctiva of clinically normal cats may be positive for FHV-1, *Chlamydia* spp., *Mycoplasma* spp. and calicivirus when evaluated by PCR, and cats with FHV-1 related ocular disease may have negative PCR results. Due to the difficulty in achieving a definitive diagnosis of the cause of infectious conjunctivitis in cats, a presumptive diagnosis may be based on the anamnesis, clinical signs and response to treatment.

Neonatal conjunctivitis, also known as ophthalmia neonatorum, is a syndrome of acute conjunctival inflammation in neonatal kittens and puppies, and manifests as copious ocular discharge, which is usually purulent. It is associated with infection, most commonly *Chlamydia* spp. or FHV-1 in cats, and *Staphylococcus* spp. or Gram-negative organisms (presumed to be faecal contaminants) in dogs or cats. If the infection develops before the natural eyelid opening at 10–14 days of age, the eyelids take on a characteristic distended appearance (Figure 10.8).



10.8 (a) Ophthalmia neonatorum with pus extruding from the medial canthus in a 7-day-puppy. (b) Note the characteristic distended appearance of the eyelids of the left eye.

KCS is a frequent cause of conjunctivitis in dogs, and is the most common cause of secondary bacterial conjunctivitis. The STT (see below) should be performed on all dogs with conjunctivitis. Allergic conjunctivitis also occurs frequently in dogs and is often accompanied by signs of atopic dermatitis. With chronicity, conjunctival lymphoid follicles develop (follicular conjunctivitis). Environmental irritants and contact hypersensitivity may cause intense chemosis, blepharoedema, severe conjunctival hyperaemia, tearing, squinting and face rubbing. Some ophthalmic medications, such as neomycin, thimerosal, benzalkonium chloride, pilocarpine, 2% dorzolamide, and prostaglandin analogues, can occasionally lead to contact hypersensitivity reactions. Acute blepharoconjunctival allergy may be included in the urticarial lesions of acute angioneurotic oedema. Lesions are characterized by the acute onset of chemosis, conjunctival hyperaemia and skin oedema involving the ears, muzzle and periorbital areas. Swelling around the eyes may be severe enough to close the palpebral fissures and prevent the animal from seeing. Urticarial blepharoconjunctivitis may be associated with insect stings, with ingestion of spoiled protein material in foods or with administration of systemic drugs.

Treatment

The treatment is based on the underlying cause of the conjunctivitis.

In cats with *Chlamydia* or *Mycoplasma* infection, topical administration of tetracycline, erythromycin, or chloramphenicol q6h for 1–2 weeks after resolution of the clinical signs is advised. In case of recurrence, oral doxycycline at 5 mg/kg q12h or 10 mg/kg q24h for 28 days or 2 weeks past resolution of the clinical signs may be needed. In the case of viral conjunctivitis, the eye should be cleaned with sterile eyewash followed by application of a suitable lubricant ointment, as well as maintenance of adequate nutrition and hydration in systemically affected animals. Every effort should be made to prevent symblepharon by breaking down any adhesions quickly and repeatedly. Given the frequent incidence of co-infections with *Chlamydia* spp. and FHV-1, topical application of tetracycline may be advised. Antiviral agents (see below) should be considered when signs are severe and persistent, and especially when there is corneal involvement.

Neonatal conjunctivitis usually resolves promptly after topical broad-spectrum antibiotic administration q4–6h. If the eyelids are still fused the lid fissure should be carefully opened without delay; otherwise, the lacrimal gland, cornea and even the whole globe can be irreversibly damaged. The fissure should be massaged until it opens. If that fails careful mechanical spreading with mosquito forceps placed into the groove of the fissure starting in the medial canthus may help open it. A sharp instrument should never be used for this purpose. A bacterial culture and susceptibility test should be performed to determine antibiotic sensitivity. The conjunctival sac should be irrigated with saline or dilute (1:50) povidone–iodine solution, and topical broad-spectrum antibiotics should be applied 4–6 times a day for as long as necessary. If the animal is younger than 10–14 days of age, the eye should be constantly lubricated with artificial tears to ensure corneal protection, since the lacrimal glands and eyelid function are still not properly developed.

Allergic and follicular conjunctivitis in dogs may be relieved by the use of intermittent topical corticosteroids, once a corneal ulcer has been ruled out with fluorescein. Urticarial blepharoconjunctivitis usually responds rapidly to intravenous or intramuscular short-acting corticosteroids such as hydrocortisone hemisuccinate (10–20 mg/kg i.v.). In cases of contact hypersensitivity reactions, the eye should be washed intensively to eliminate any chemical residues.

If KCS is diagnosed, appropriate longer term treatment should be started. For a detailed description of the causes of KCS and related treatment, an ophthalmology textbook should be consulted (Giuliano, 2013; Miller, 2013a; Gould and McLellan, 2014).

Prognosis

The majority of cases of conjunctivitis in dogs and cats have a good prognosis with appropriate treatment. However, many cases of allergic and viral or bacterial conjunctivitis are recurrent. Owners should be warned of this because many become frustrated when the disease returns. An ophthalmologist should be consulted in recurrent or non-responsive cases.

Corneal ulcers

Definition

A corneal ulcer is any keratopathy in which there is loss of epithelium with exposure of the underlying corneal stroma. Corneal ulcers are classified by the depth of corneal involvement and by their underlying cause. The most common causes of corneal ulcers are listed in Figure 10.9.

- Trauma/abrasions
- Keratoconjunctivitis sicca
- Foreign bodies
- Infection (bacterial, viral, fungal)
- Exposure keratitis (e.g. due to an anatomical abnormality or nerve damage (facial nerve paralysis, trigeminal nerve paralysis))
- Topical irritants
- Entropion
- Trichiasis
- Distichiasis
- Ectopic cilia
- Dermoid
- Eyelid agenesis
- Eyelid neoplasia or inflammation

10.9 Causes of corneal ulcers.

Clinical signs and initial evaluation

Patients with corneal ulcers usually present with lacrimation, blepharospasm, photophobia, conjunctival hyperaemia, corneal oedema, and possibly miosis and aqueous flare.

Unless imminent danger of perforation is suspected or excess tearing is observed, a STT (Figure 10.10) should be performed to rule out KCS as the underlying cause. The eye should be thoroughly examined for any eyelid and/or conjunctival anatomical or functional abnormality (e.g. entropion, ectopic cilia, trichiasis, distichiasis, lagophthalmos), as well as for any foreign body under the nictitating membrane and eyelids. Fluorescein stain should be applied to diagnose and characterize the ulcer. Microbiological assessment and cytological examination of corneal samples should be performed if the ulcer is suspected to be infected.

The Schirmer tear test (STT) measures the amount of aqueous tears produced in 1 minute using a strip of 5 x 35 mm filter paper. The most common is the Schirmer tear test (STT-1), which is performed in an unanaesthetized eye, before any medications are administered. This measures the basal and reflex tear production. In dogs, normal STT-1 values range from 15–25 mm/min. Readings of less than 10 mm in 1 minute are considered diagnostic for KCS and values between 10 and 15 mm in 1 minute are considered highly suggestive of KCS. In cats, normal STT-1 values range from 9–34 mm/min. Readings of less than 9 mm in 1 minute in conjunction with appropriate clinical signs (e.g. tacky mucoid discharge, conjunctival hyperaemia and thickening) are considered diagnostic for KCS.

The STT-1 is easy to perform and can be done in most animals with minimal restraint. The strips have millimetre scale markings on them to facilitate the measurement. The strips should not be taken out of the package until the operator is ready to perform the test, and the test area of the strip should never be touched.

1. While the test strip is still in the package, the strip is folded at the notch so that the end is perpendicular to the rest of the strip.
2. The folded part of the strip is placed in the ventrolateral conjunctival sac so that the notch rests at the eyelid margin.
3. The strip is held in place for 1 minute, and the tears produced flow down the test strip.
4. If necessary, the eyelids can be gently held closed to keep the strip in place.
5. The STT should be performed in both eyes.



10.10 Schirmer tear test.

Basic management

The most important step is identification and removal or correction of the cause. Without this step, ulcers will not heal and may progress.

Topical antibiotics are indicated for all corneal ulcers since disruption of the epithelium predisposes the corneal stroma to infection.

Stimulation of the abundant pain receptors in the cornea by ulceration can induce a neurogenic reflex anterior uveitis, which causes miosis and increased protein levels in the aqueous humour (aqueous flare) and exacerbates the pain associated with ulceration. Topical application of a mydriatic and cycloplegic agent (e.g. atropine, cyclopentolate) is therefore justified in most cases of corneal ulceration. Topical atropine may significantly decrease tear production, and thus should be avoided in patients with corneal ulcers and borderline low or decreased tear production since it will exacerbate the dryness and complicate the ulcerative disease. Cyclopentolate may be used in those cases.

Topical corticosteroids are always contraindicated because they predispose to infection, delay corneal healing, and potentiate enzymatic destruction of the cornea. Topical NSAIDs may be used instead; however, they may also delay corneal healing and use of such agents has been associated with devastating ulcer progression in some humans with infected ulcers (Bekendam *et al*., 2007; Feiz *et al*., 2009). Therefore, topical NSAIDs should be used with discretion and avoided in the presence of infected ulcers. If moderate to severe uveitis accompanies the ulcer, systemic NSAIDs can be used.

Another important therapeutic consideration, especially in dogs, is prevention of self-trauma with the use of an Elizabethan collar.

If more than one eye drop drug formulation is needed, a period of at least 10 minutes should be interposed between administration of different medications. If both drops and ointments are being used, the eye drop should be given before the ointment or at least 2 hours after ointment application.

Monitoring

For all ulcers, regardless of the treatment, owners should monitor the eye carefully. Urgent re-evaluation is warranted if: there is a discharge from the cornea; the animal starts to keep its eye closed; the eye appears more red or pain recurs; the eye loses or changes shape; or the animal becomes lethargic or anorexic. Brachycephalic breeds with macroblepharon are very susceptible to central corneal ulcers. These ulcers can progress rapidly and require particularly careful monitoring.

Superficial ulcers

Although superficial ulcers are severely painful and frequently present as emergencies, they usually are not a threat to vision at this point.

Diagnosis

Superficial ulcers are diagnosed based on fluorescein stain retention, and are relatively clear defects in the cornea (Figure 10.11).

Treatment

Treatment includes topical antibiotics. Triple antibiotic solution (neomycin and polymyxin B along with bacitracin or gramicidin), chloramphenicol or oxytetracycline q6–8h is usually sufficient. As anaphylactic reactions have been reported in cats after topical application of triple antibiotic medications, some clinicians avoid their use in simple superficial ulcers. However, many ophthalmologists have used triple antibiotic ophthalmic medications without complications. Atropine sulphate 1% or cyclopentolate may also be used if a miotic pupil is present or the eye is painful (due to ciliary muscle spasm). They are usually applied q12–24h with rapid tapering of dose frequency as analgesia and adequate pupil dilation are achieved.

The underlying cause of the ulcer must be identified and treated.

In cases of chemical-induced ulcers, the nature of the chemical should be identified. Acids tend to denature proteins on contact, limiting their penetration through the cornea; alkaline agents may rapidly penetrate the cornea, and enter the anterior chamber. The eye should be copiously irrigated with sterile lactated Ringer's (Hartmann's) solution. However, if lactated Ringer's solution is not available, sterile saline or water is still beneficial, since the most important treatment of the chemically injured cornea is dilution of the chemical agent. Keratomalacia is an important complication of chemical- induced ulcers and thus the application of topical anticollagenases (see below) is recommended.

If KCS is the initiating cause of the ulcer, appropriate treatment for KCS should also be started and topical atropine must be avoided since it will exacerbate the dryness and complicate the ulcerative disease.



10.11 (a) Superficial corneal ulcer in a dog caused by a chemical burn with an alkaline agent (caustic soda). Note the severe corneal oedema limited to the ulcerative area, the conjunctival hyperaemia, and the burn lesions on the eyelid margins. The eye was copiously irrigated with sterile lactated Ringer´s solution and was treated topically with one drop of atropine, ofloxacin q6h, oxytetracycline (anticollagenase) q6h and an oral NSAID q24h. The ulcer was completely healed 1 week later. (b) The same eye 1 month later.

In cats, many corneal ulcers have a viral (FHV-1) aetiology. If the history and clinical signs are consistent with FHV-1 infection, a topical antiviral medication (ganciclovir, 4–6 times a day; cidofovir, 2 times a day) can be included in the treatment. Oral famciclovir at a dose of 90 mg/kg q12h can be administered instead.

If moderate to severe uveitis accompanies the ulcer, systemic NSAIDs can be used.

The eye should be re-stained after 4–6 days, at which time the ulcer should be healed. If not, it should be re-evaluated for an undetected, underlying cause or contributing factor.

Prognosis

If there are no complications and the underlying cause is corrected, the prognosis is excellent.

Spontaneous chronic corneal epithelial defects

Diagnosis

Spontaneous chronic corneal epithelial defects (SCCEDs), also known as indolent ulcers, are a specific type of ulcer that occurs in dogs. SCCEDs are characterised to be superficial, non-healing ulcers with redundant, non-adherent corneal epithelial margins. Histopathologic evaluation of affected corneal samples demonstrate the presence of a hyaline acellular zone within the superficial stroma. This hyaline zone is theorized to interfere with the normal healing process of the cornea causing failure of the attachment between the epithelium and the underlying stoma. Although more common in the Boxer breed, this type of ulcer should be considered in any middle-aged to old dog with evidence of chronic ulceration despite presentation as an acute emergency. When the ulcer is stained with fluorescein, the stain extends further than the visible edges of the ulcer, demonstrating an area of epithelium that has not anchored to the stroma. Although these ulcers are generally chronic, they often present as an emergency due to the waxing and waning of blepharospasm and the moderate to intense vascularization that the client may observe.

Treatment

A topical anaesthetic (e.g. proparacaine) is placed on the eye. The area around the ulcer is gently debrided with a sterile cotton swab to elevate and remove the loose epithelium unattached to the underlying stroma. A diamond burr device is then used to perform a superficial corneal debridement. This relatively new technique is considered efficient and safe, is easily performed, and has been compared favourably with other techniques (da Silva *et al*., 2011; Gosling *et al*., 2013; Dawson *et al*., 2017).

Alternatively, a grid or punctate keratotomy can be performed using a 25 G needle, to gently break the superficial hyaline zone while avoiding going through the stroma. To perform punctate keratotomy, the needle is grasped with a haemostat so that the tip of the needle is barely exposed which improves control of penetration depth. The keratotomy must extend 1 mm into the normal surrounding attached epithelium. Sedation is recommended for fractious dogs and for clinicians inexperienced with this technique.

The use of a bandage contact lens is advocated in many instances to promote healing time and patient comfort.

A topical antibiotic (e.g. triple antibiotic solution (neomycin and polymycin B along with bacitracin or gramicidin), chloramphenicol or oxytetracycline q6–8h) and atropine or cyclopentolate (q12–24h, until effect) should be administered. Systemic administration of NSAIDs is often indicated to reduce pain associated with neurogenic reflex anterior uveitis. It is recommended that the eye is checked every 7–14 days. Debridement and keratotomy may need to be repeated. A superficial keratectomy is 100% effective as a surgical treatment for SCCEDs, and should be recommended in refractory cases. This requires general anaesthesia and an operating microscope, and should be performed by a veterinary ophthalmologist.

Prognosis

With appropriate treatment, the majority of SCCEDs heal successfully.

Stromal ulcers

Diagnosis

Stromal ulcers are also diagnosed based on fluorescein staining, although the defect may be appreciated on gross examination (Figure 10.12). Deep ulcers may not be as painful as superficial ulcers and they usually involve a secondary microbial infection. Microbiological assessment and cytological examination of corneal samples should be performed if the ulcer is suspected to be infected (gelatinous appearance to the ulcer bed or presence of cellular infiltrate). Cytology allows rapid identification of bacteria (cocci or rods), fungal hyphae and yeasts and characterizes the type of inflammatory process that may guide the immediate course of therapy. It is performed under topical anaesthesia using a cytrobrush, a kimura spatula or the blunt end of a scalpel to gently scrape the cornea at the affected area. In case of deep or melting corneal ulceration, in which excessive manipulation may be contraindicated, cotton-tipped swabs are the least traumatic method to obtain a sample. The cytological preparation should be stained with Romanowsky-type stains (e.g. Diff-Quik®) and/or Gram stain.

Treatment

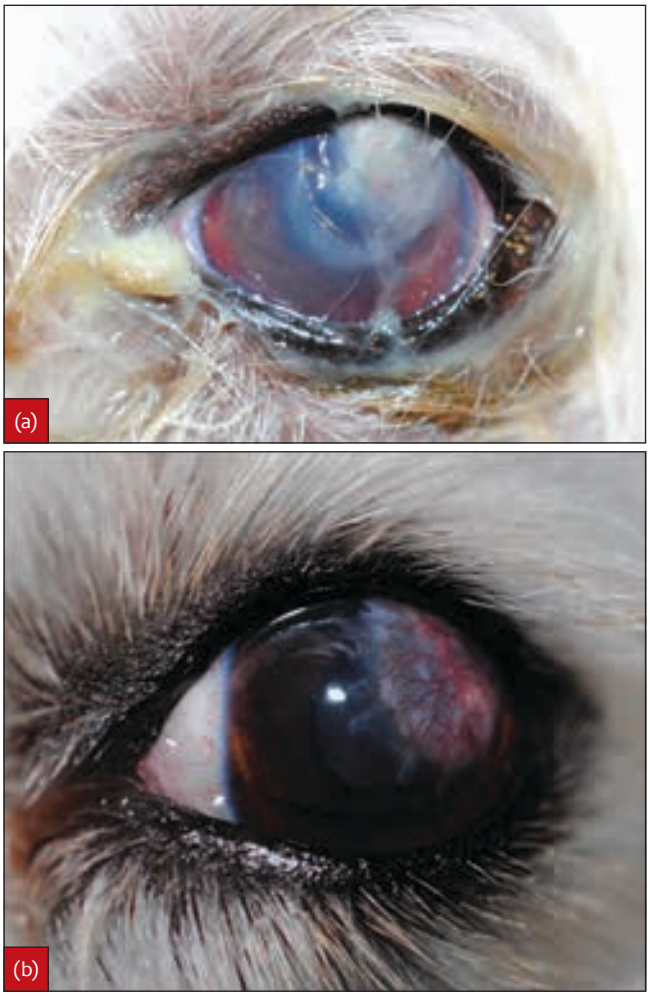
Non-progressive stromal ulcers can be treated similarly to superficial ulcerations. Progressive deep stromal ulcers, as indicated by increasing depth and width of the ulcer, a gelatinous appearance to the ulcer bed or the presence of cellular infiltrate are potentially vision- and globe-threatening, and therapy must be more aggressive. Antibiotic selection is frequently made on the basis of cytology and culture and sensitivity results. Initial topical therapy with a broad-spectrum antimicrobial such as a late-generation fluoroquinolone (e.g. moxifloxacin, gatifloxacin) or combination therapy with an early-generation fluoroquinolone (e.g. ciprofloxacin, ofloxacin) or aminoglycoside (e.g. tobramycin), in addition to chloramphenicol or triple antibiotic, should be administered every 4 hours.

Topical atropine sulphate 1% or cyclopentolate should be administered to minimize the discomfort from the ciliary muscle spasm and to reduce the risk of synechiae formation. They are usually applied q12–24h with rapid tapering of dose frequency as analgesia and adequate pupil dilation are achieved.

If rapid stromal loss or melting is present (Figure 10.13a and 10.14), more aggressive antibiotic therapy (q2–4h) is needed in the first 48 hours. Thereafter the application can usually be reduced every 4–6 hours. Certain bacteria (especially Gram-negative rods), inflammatory cells and damaged corneal stromal or epithelial cells produce collagenases and proteases, which can rapidly destroy (melt) the cornea. A topical antiproteinase-anticollagenase should also be added to the treatment regimen in patients with melting ulcers. Autologous serum can be used, in which alpha-2-macroglobulin and alpha-1-proteinase inhibitor act as antiproteinases. Tetracyclines inhibit metalloproteinases and other mediators of inflammation that lead to melting ulcers. Autologous plasma, acetylcysteine 4–5% or disodium ethylenediaminetetraacetic acid (EDTA) 0.2% may also be used. Antiproteinases-anticollagenases should be instilled every 1–2 hours until healing is well underway.



10.12 (a) Deep corneal ulcer in a Shih Tzu caused by an ectopic cilium on the upper lid. (b) Two ectopic cilia can be observed on the upper lid (arrow and arrowhead); the ulcer was caused by the ectopic cilium located in the centre (arrowed).



10.13 (a) Melting corneal ulcer in a dog. The ulcer was deep, affecting more than two-thirds of the corneal thickness, and thus a combination of surgical and medical treatments was performed. (b) The eye 1 month after placement of a pedicle conjunctival graft.



10.14 Melting corneal ulcer in a cat.

Thereafter, the application can be reduced to every 4–6 hours. Systemic administration of NSAIDs is usually indicated to reduce corneal inflammatory cell infiltration (and associated stromal loss) and pain associated with neurogenic reflex anterior uveitis. Most systemically administered antibiotics do not achieve therapeutic concentrations in the cornea because it is avascular. However, they may be indicated in vascularized corneas. Oral doxycycline (5 mg/kg q12h) is usually selected due to the anti-inflammatory and immunomodulatory additive effects.

For all deep ulcers, care must be taken to avoid excessive restraint of the patient, as this can lead to perforation. An Elizabethan collar must be worn to protect against self-trauma. The eye should be monitored very carefully for the first 1–2 days, to ensure that the ulcer is healing properly. Surgical intervention is indicated when the depth of the corneal lesion is more than 50% of the corneal thickness or if the ulcer is progressing despite aggressive medical therapy. Surgical procedures most commonly employed in these cases include grafts of conjunctiva (see Figure 10.13b), amniotic membrane (or other biomaterials) and cornea, and corneoconjunctival transposition. An ophthalmologist should be consulted for corneal grafting procedures since surgical success requires microsurgical skills, fine suture material, and high magnification.

Prognosis

With early and appropriate medical and/or surgical treatment, the prognosis for vision and the globe can be good to fair depending on the extent and severity of the corneal disease.

Descemetocele

Diagnosis

A descemetocele is a deep corneal ulcer in which the corneal epithelium and stroma have been completely destroyed, leaving a lesion lined only by Descemet's membrane and corneal endothelium. The base of such ulcers is typically clear and the elasticity of Descemet's membrane may cause it to bulge anteriorly. Although the walls of the ulcer (stroma) will be fluorescein-positive, the base (Descemet's membrane) will not take up the stain (Figure 10.15). In this case, the cornea is in imminent danger of perforation.



10.15 Central corneal descemetocele in a dog with keratoconjunctivitis sicca and distichiasis. Note the fluorescein uptake in the periphery of the ulcer. The base (Descemet's membrane) does not take up the stain.

Treatment

A descemetocele is a true emergency and should be managed by a combination of surgical and medical therapy. Topical antibiotics should be started as indicated for deep corneal ulcers. Ointments should be avoided when there is a risk of corneal perforation because of the irritating properties of white petrolatum and mineral oil, which may lead to severe granulomatous uveitis if rupture does occur. An Elizabethan collar, cage rest and gentle restraint are important. Great care must be taken to prevent pressure on the globe, to avoid the risk of corneal perforation. If the animal is struggling or resents restraint, medications should wait until after surgical repair, as long as this can be performed immediately.

Most small descemetoceles (e.g. less than 5 mm in diameter) can be repaired successfully using conjunctival grafts; however, the corneal lesion will remain fragile and may develop a large stromal scar. Use of cornea or another tissue that has more structural integrity than conjunctival tissue alone is preferred. A corneoconjunctival transposition or grafting procedures with cornea or biomaterials, alone or in combination with a conjunctival graft, may be used. An ophthalmologist should be consulted for corneal grafting procedures since surgical success requires microsurgical skills, fine suture material and high magnification.

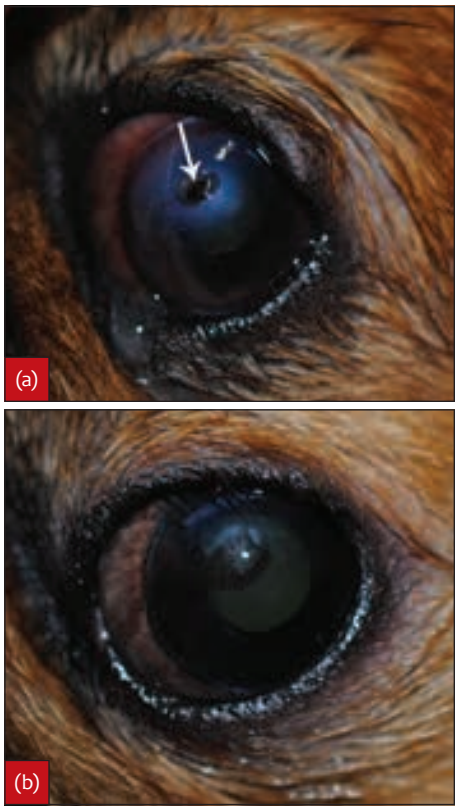
Prognosis

If surgical repair can be performed and no complications are encountered, the prognosis for the globe can be good. Prognosis for vision depends on the extent of corneal disease and the type of graft chosen for surgical repair.

Corneal perforation

Diagnosis

Following corneal perforation, aqueous humour is lost, iris prolapse may occur (Figure 10.16a) and/or the cornea may seal with a fibrin clot or continue to leak aqueous humour, causing collapse of the anterior chamber. A misshapen cornea or decreased depth of the anterior chamber may also be seen. To determine whether the defect is sealed, a



10.16 (a) Corneal perforation in a Pekingese. Note the small iris prolapse at the centre of the corneal lesion (arrowed). (b) The eye 6 weeks after surgical replacement of the iris into the anterior chamber followed by a corneoconjunctival transposition.

Seidel test may be performed by applying a drop of fluorescein directly on the cornea. Without irrigating the eye, it should be observed if the aqueous forms rivulets at the site of perforation (positive Seidel test).

Treatment

A corneal perforation should be considered a surgical emergency because of the risk for infection and intraocular inflammatory damage. If the menace response is negative, evaluation of the dazzle reflex and consensual PLR may provide some information regarding the integrity of the posterior segment. The presence of these reflexes is a positive clinical sign. Absence of the consensual pupillary light and dazzle reflexes indicates a poor prognosis, and in such case, a transpalpebral (through the closed lids) ocular ultrasound examination should be performed to assess the posterior segment. If a retinal detachment (RD) is observed enucleation should be considered.

Systemic broad-spectrum antibiotics and NSAIDs should be added to the protocol to help control infection and inflammation. The animal must be kept calm and ideally rested in a cage to help prevent the clot from dislodging and rupturing the eye. An Elizabethan collar must be worn to protect against self-trauma. Great care must be taken to prevent pressure on the globe, to avoid the risk of further intraocular damage. Topical antibiotic solutions are indicated, as for deep corneal ulcers. If the cornea is leaking, consideration should be given to the potential risk that the preservatives the antibiotic solutions contain may cause damage to intraocular structures; however, the benefits of preventing bacterial infection are likely to outweigh the risks. Ointments are contraindicated as they may lead to severe granulomatous uveitis due to the irritating properties of white petrolatum and mineral oil.

Conjunctival grafts do not have adequate structural integrity to maintain a watertight seal and a formed anterior chamber after surgery. For this reason they are not considered an ideal option as a surgical treatment alone for corneal perforation. A corneoconjunctival transposition (see Figure 10.16b) or grafting procedures with cornea or biomaterials, alone or in combination with a conjunctival graft, may be used.

Prognosis

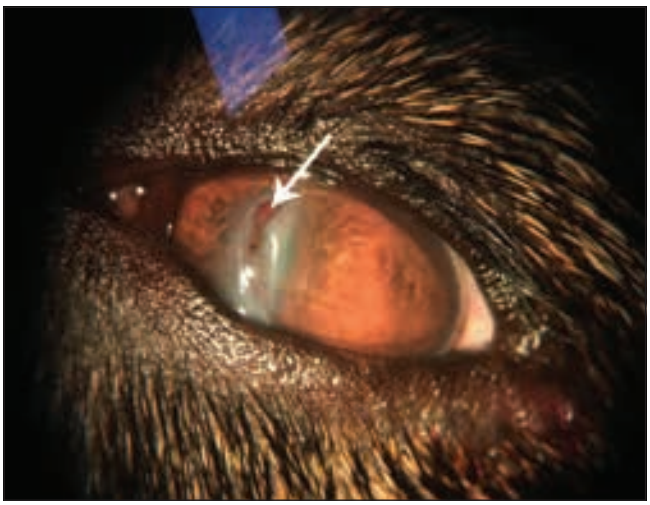
If surgical repair can be performed and no complications are encountered, the prognosis for the eye is good and the prognosis for return of normal vision is good to reserved, depending on the extent of the corneal disease and the type of graft chosen for surgical repair.

Corneal lacerations

Diagnosis

Clinical signs depend on the extent and depth of the wound and are similar to those seen with corneal ulcers or corneal perforation (in the case of full-thickness laceration) (Figure 10.17). Corneal lacerations usually occur as a consequence of sharp trauma. Blunt trauma can also cause globe rupture; however, this tends to be along the limbus rather than dissecting across the central cornea.

The eye should be carefully evaluated to determine the extent of the corneal damage and intraocular injury. Great care must be taken to prevent pressure on the globe, to avoid the risk of further intraocular damage. The animal may need to be sedated to prevent further damage to the eye and allow a closer examination. Deflation of the anterior chamber, iris prolapse, hyphaema, hypopyon and significant corneal oedema may prevent a complete ophthalmic examination. Consensual pupillary light and dazzle reflexes are positive clinical signs. Absence of the consensual pupillary light and dazzle reflexes indicates a poor prognosis, and in such case a transpalpebral ocular ultrasound examination should be performed to assess the posterior segment. If retinal detachment is observed enucleation should be considered. If the laceration involves penetration of the eye (e.g. due to a cat claw) that reaches or disrupts the capsule of the lens, a very intense, severe anterior uveitis and cataract can ensue.



10.17 Full-thickness corneal laceration in a dog resulting from a cat claw injury. Note the corneal oedema around the edges and a fibrin clot sealing the full-thickness defect (arrowed).

Treatment

If the laceration is less than 50% of the corneal thickness, it should be treated medically as a corneal ulcer. Lacerations that are deeper than 50% of the corneal thickness or perforate through the cornea (full-thickness laceration) usually require primary suturing or grafting procedures and should be referred immediately to a veterinary ophthalmologist. Surgical repair of an iris prolapse may involve resection of exposed unviable iris or replacement of viable iris into the anterior chamber, followed by closure of the remaining full-thickness wound. If the lens capsule is disrupted, prophylactic lensectomy, (phacoemulsification) may be also indicated. Before referral, an Elizabethan collar must be placed and systemic broad-spectrum antibiotic and anti-inflammatory treatment should be administered. If severe anterior uveitis is observed and lens disruption is suspected, the topical application of NSAIDs such as ketorolac or nepafenac (q8h) is also recommended.

Prognosis

The prognosis depends on the extent and depth of the corneal laceration, duration of the injury and the severity of intraocular injury. If severe intraocular damage is not present, and prompt and adequate treatment is performed, the prognosis is good.

Corneal foreign bodies

Diagnosis

The ocular signs range from minimal ocular discomfort to signs of significant ocular pain, including blepharospasm, blepharoedema, enophthalmos and tearing. Conjunctival hyperaemia may be present and fluorescein dye uptake and corneal oedema are likely to be seen surrounding a corneal foreign body.

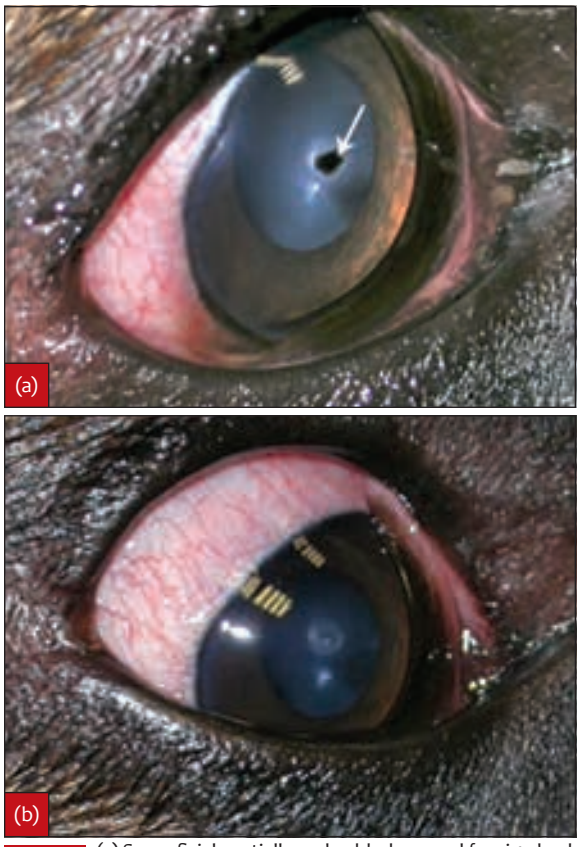
Superficial corneal foreign bodies may be associated with minimal anterior uveitis, whereas deep or penetrating foreign bodies will be accompanied by significant miosis, flare, hypopyon and/or hyphaema. The foreign body may be adhered to the corneal surface and firmly attached, creating an ulcerative region, or may penetrate into the cornea or into the globe itself (Figure 10.18). Corneal foreign bodies are usually obvious. However, magnification or slit lamp examination may be necessary to locate and assess the depth of smaller objects and to distinguish between foreign bodies that remain within the cornea and foreign bodies tracts, as blood or debris within the tract can mimic the presence of a foreign body.

The eye should be carefully evaluated to determine the extent of the corneal damage and possible intraocular injury.

Treatment

Treatment depends on the depth of the foreign body and the severity of secondary ocular injuries.

Superficial foreign bodies are usually removed under topical anaesthesia by vigorous irrigation with sterile saline or using a 25 G needle to 'flick' the foreign body out taking care not to push it further into the stroma. Deeper stromal and penetrating foreign bodies should be referred for surgical removal under general anaesthesia and magnification with an operating microscope.



10.18 (a) Superficial partially embedded corneal foreign body. Note the conjunctival hyperaemia and perilesional corneal oedema surrounding the foreign body (arrowed). This was a piece of plant material that was gently removed using a 25 G needle. (b) The eye following removal of the foreign body.
(Courtesy of C Peruccio)

After removal, a topical broad-spectrum antibiotic and atropine or cyclopentolate should be administered to control infection and limit the effects of secondary uveitis. If moderate to severe uveitis is present or globe perforation has occurred, topical and systemic NSAIDs can be used. In cases of globe perforation systemic antibiotics are also indicated. Close monitoring of the eye for potential complications such as progressive ulceration, infection (bacterial and/or fungal) or abscess is required.

Prognosis

The prognosis for eyes with superficial corneal foreign bodies is good, provided the foreign body is removed and infection is avoided. The prognosis for deep and penetrating foreign bodies depends on the extent and depth of the corneal damage and intraocular injury (e.g. severity of uveitis and lens trauma).

Glaucoma

Definition, pathophysiology and causes

Glaucoma is a group of ocular diseases that result in progressive retinal ganglion cell (RGC) death and optic nerve degeneration. An increase in IOP is the main risk factor in the development of glaucoma in veterinary patients.

IOP results from a balance between aqueous humour production and its outflow. The aqueous humour is present in the anterior segment of the eye. It is produced in the

posterior chamber by the non-pigmented epithelium of the ciliary body through three basic mechanisms: active secretion, diffusion, and ultrafiltration. Active secretion is the principal mechanism of aqueous humour formation (80–90%) and it is mainly catalyzed by the enzyme carbonic anhydrase (50–60%). Aqueous humour circulates from the ciliary body through the pupil and into the anterior chamber. From here it travels peripherally to the iridocorneal angle (the junction of the base of the iris and cornea) and ciliary cleft to reach the venous system (so-called conventional outflow route). A small percentage of the aqueous humour is also drained by the stroma of the iris, ciliary body and choroids to reach the venous system (unconventional or uveoscleral outflow route).

Glaucoma is triggered by an initial event that obstructs aqueous humour outflow from the anterior chamber. Blockade of aqueous humour drainage leads to an increase in IOP. As the elasticity of the eye is limited, the progressive increase in IOP impairs blood flow and axoplasmic flow of the optic nerve. This leads to a cascade of biochemical changes that induces RGC dysfunction, resulting in optic nerve degeneration and atrophy, visual field loss and blindness.

Glaucoma can be classified according to its aetiology as congenital, primary or secondary (Figure 10.19) Congenital glaucoma is rare in dogs and cats and is usually associated with considerable developmental abnormalities of the aqueous humour outflow route. In primary glaucoma, the IOP increase is not associated with any other ocular disease. It is associated with changes in the iridocorneal angle and is hereditary in many breeds (Figure 10.20); it is a bilateral disorder, although it does not usually develop simultaneously in both the eyes. According to the morphology of the iridocorneal angle it can be classified as open angle, narrow angle, closed angle, and with goniodysgenesis (consolidation of adjacent pectinate ligaments into broad sheets). Age of presentation varies by breed but is generally between 4 and 10 years of age. In secondary glaucoma, the IOP increase is associated with a concurrent ocular disease that physically blocks aqueous humour outflow. The obstruction can be localized in the iridocorneal angle or pupil. Secondary glaucoma frequently occurs as a consequence of anterior uveitis, lens luxation, cataracts (lens-induced uveitis or intumescent cataracts), hyphaema and intraocular tumours. Secondary glaucoma represents the most common type of glaucoma in cats.

Primary
• Open angle/cleft • Narrow/closed angle/cleft • Pectinate ligament dysplasia/goniodysgenesis
Secondary
• Anterior uveitis[a] • Lens luxation or subluxation • Cataract • Aphakic • Hyphaema • Intraocular neoplasia[a] • Malignant/aqueous misdirection • Melanocytic glaucoma • Pigmentary and cystic glaucoma in Golden Retrievers • Postoperative ocular hypertension • Giant retinal tears
Congenital glaucoma

10.19 Common causes of primary and secondary glaucoma. [a] Most common causes of glaucoma in cats.

- Alaskan Malamute
- American Cocker Spaniel
- Australian Cattle Dog
- Basset Fauve de Bretagne
- Basset Hound
- Beagle
- Boston Terrier
- Bouvier des Flandres
- Bullmastiff
- Chow Chow
- Dalmatian
- English Cocker Spaniel
- English Springer Spaniel
- Entlebucher
- Eurasier
- Flat-coated Retriever
- Fox Terrier, Smooth and Wire
- Golden Retriever
- Great Dane
- Jack Russell Terrier
- Labrador Retriever
- Leonberger
- Newfoundland
- Norwegian Elkhound
- Petit Basset Griffon Vendéen
- Poodle
- Samoyed
- Shar-pei
- Shiba Inu
- Siberian Husky
- Welsh Springer Spaniel
- Welsh Terrier

10.20 Dog breeds affected by primary glaucoma.

Clinical signs

The clinical signs depend on the stage, the cause of glaucoma and the species. Early, non-congestive glaucoma characterizes the early stages of primary glaucoma. The clinical signs are insidious and often undetected, with values of IOP mildly increased. Acute congestive glaucoma is associated with sudden and severe spikes in IOP, and usually manifests with signs of pain (tearing, blepharospasm, depression, lethargy), redness (due to episcleral vessel engorgement), corneal oedema, sluggish PLR or dilated pupil, and decreased to absent menace response (Figure 10.21). Chronic glaucoma can also lead to buphthalmia (enlarged globe), exposure keratopathy, corneal



10.21 Acute primary glaucoma (narrow angle) in an English Cocker Spaniel. Note the redness (due to conjunctival hyperaemia and episcleral congestion), diffuse corneal oedema and mydriasis. The intraocular pressure is 64 mmHg.

striae, lens luxation or subluxation, retinal degeneration and cupping of the optic disc, and almost invariably results in blindness. Signs of pain and redness tend to become less apparent in eyes with chronic glaucoma. In secondary glaucoma, other clinical signs can also be seen depending on the aetiology (e.g. anterior uveitis, lens luxation, cataracts, intraocular tumours, hyphaema).

Due to the differences in the anatomy and physiology of the feline eye, clinical signs of glaucoma in cats are slightly different. Moderate elevations of IOP are associated with few overt clinical signs and acute painful glaucoma is rarely seen in cats. Cats with glaucoma seldom show obvious signs of discomfort, even in the face of a very high IOP. Conjunctival hyperaemia and corneal oedema are usually not seen until the late stages of the disease. Vision is also maintained for a much longer time than in dogs. For these reasons, cats are usually presented when glaucoma has reached a chronic stage.

Diagnosis

The IOP should be measured using an applanation (TonoPen) or rebound (TonoVet) tonometer (Figure 10.22). Both instruments are very reliable; however, according to recent studies the rebound tonometer appears to have superior accuracy in both dogs and cats. Use of a Schiøtz tonometer is no longer recommended due to unreliability of readings and challenges in performing the technique well.

Normal IOP is approximately 12–25 mmHg in dogs and 12–27 mmHg in cats. IOP values exceeding 25 mmHg in dogs and 27 mmHg in cats in conjunction with compatible clinical signs are indicative of glaucoma. IOP values greater than 20 mmHg are suspicious for glaucoma if other clinical signs, or anterior uveitis, are present, or if the patient is being treated for glaucoma.

A critical ophthalmic examination should be performed to detect or rule out any ocular abnormality that may cause secondary glaucoma.

Gonioscopy is the examination of the iridocorneal angle and ciliary cleft. After the application of topical anaesthesia and with minimal restraint, a specific lens is placed on the corneal surface and the iridocorneal angle is inspected usually using a biomicroscope. This allows the clinician to differentiate between open angle, narrow angle and closed angle glaucoma, with or without goniodysgenesis. In secondary glaucoma, gonioscopy may also help to visualize infiltration of the iridocorneal angle by inflammatory cells, neoplastic or inflammatory masses or pigment deposition. Considerable practice is, however, necessary for a correct interpretation, and hence gonioscopy tends to be performed almost exclusively by veterinary ophthalmologists.

Examination of the ocular fundus by direct and/or indirect ophthalmoscopy is very important as it provides information that aids in staging the glaucoma and giving a prognosis for vision. In acute glaucoma, the optic disc may appear swollen with an adjacent peripapillary ring of retinal oedema. Within 24–48 hours the increased pressure may cause the disc to appear pale and compressed (cupping). In advanced glaucoma, increased tapetal reflectivity due to retinal atrophy may be seen, together with attenuation or complete loss of retinal vessels, and optic nerve atrophy.

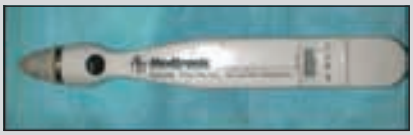
In cases with severe diffuse corneal oedema or any other opacity that precludes complete intraocular examination, ocular ultrasonography should be performed to examine the anterior and posterior segment and possibly determine the aetiology of glaucoma (e.g. intraocular mass, lens luxation, uveitis, retinal detachment).

Treatment

Acute glaucoma is an emergency. Early identification of the cause and rapid reduction of IOP are essential to prevent permanent blindness. Emergency treatment involves the use of agents that rapidly decrease IOP to values less than 20 mmHg.

Applanation tonometer

The Tonopen tonometer estimates IOP by measuring the force required to flatten (applanate) a small area of the corneal surface.



1. Topical anaesthetic is placed in both eyes.
2. A condom is placed on the probe of the tonometer.
3. The probe is gently tapped on the central cornea multiple times without causing visible identation. On each successful 'tap', a brief beep sounds, signaling that an individual reading was obtained.
4. A sustained tone indicates when a mean IOP has been calculated. The mean IOP is then shown on the display.
5. The reliability (coefficient of variance) of the result should be 5%, or tonometry should be repeated

The applanation tonometer can be used with the animal in a normal standing position and can be used after intraocular surgery.

Rebound tonometer

The TonoVet tonometer utilizes an impact method to determine IOP. It injects a small probe at a fixed distance from the cornea and assesses the motion of the probe as it strikes the cornea and returns (rebounds) to the instrument. The measurement should be obtained without the use of topical anesthesia.



1. The tip off the probe should be positioned perpendicular to the corneal surface at a distance of 4–8 mm.
2. The measurement button should be lightly pressed. The tip of the probe should hit the central cornea. Six measurements are made consecutively. After each successful measurement there is short beep. After the six measurements, there is a longer beep and the IOP is shown on the display.

The rebound tonometer can be used with the animal in a normal standing position and can be used after intraocular surgery.

10.22 Tonometry is the measurement of IOP. The most frequently used techniques include applanation and rebound tonometry. For accurate readings and in order to avoid erroneous overestimations of IOP, the animal should be resting quietly and the eye lids should be opened from over the bony orbital rim thereby avoiding pressure on the globe. The IOP should be measured in both eyes.

Topical prostaglandin analogues (PGAs), including latanoprost, travoprost and bimatoprost, increase the drainage of aqueous humour through both unconventional and conventional outflow. They are the first-line drugs in the emergency management of acute primary glaucoma in dogs. They can rapidly decrease the IOP by 60% and should be administered twice daily. They should, however, be used with caution in dogs with glaucoma secondary to anterior uveitis, because of their potential to exacerbate the inflammatory process. They also induce a severe miosis, which in cases of uveitis may predispose to posterior synechiae. They are contraindicated in glaucoma secondary to anterior lens luxation, since as a consequence of their miotic effect they may potentiate pupillary block, further worsening the glaucoma. Their effect in decreasing IOP is limited in cats.

Carbonic anhydrase inhibitors (CAIs) decrease the volume of aqueous humour produced. Topical CAIs (2% dorzolamide and 1% brinzolamide) decrease the IOP significantly and can be used in every type of glaucoma both in cats and dogs q8–12h. Oral CAIs (acetazolamide, methazolamide, dichorphenamide) are not more effective than topical CAIs and can induce side effects including anorexia, nausea, vomiting, diarrhoea, hypokalaemia and possible hyperventilation secondary to metabolic acidosis. Combined application of topical and systemic CAIs has no additional IOP-decreasing effects.

Timolol maleate, a topical beta-blocker, can be used in dogs and cats in combination with a topical CAI to further decrease the volume of aqueous fluid produced. Despite being applied topically, systemic absorption may cause significant cardiorespiratory effects such as bradycardia, hypotension, and bronchospasm. Therefore, it should never be administered more than twice daily, especially in smaller patients, and its use is contraindicated in patients with cardiac and respiratory disorders. Timolol should be used with caution in dogs and cats with uveitis or pupil block glaucoma (e.g. anterior lens luxation) because it may cause miosis. A fixed combination of 2% dorzolamide and 0.5% timolol is currently available in Europe and the USA.

Mannitol, the most frequently used osmotic agent, is only used for the emergency treatment of acute glaucoma. It increases the osmolarity of the extracellular fluids thereby helping reduce the IOP in two ways. Firstly, it draws water from the vitreous body into the vasculature and secondly, it leads to a slight reduction in aqueous humour production by inhibiting the ultrafiltration process in the ciliary body. It can be given at a dose of 1–2 g/kg i.v. over 20–30 minutes. This therapy can lower the IOP within 0.5–1 hour and the effect may last up to 6–10 hours. The dose can be repeated after 4 hours if the IOP does not decrease below 30 mmHg; long-term use should be avoided. If the animal is well hydrated and perfused, water should generally be withheld for up to 4 hours following the use of mannitol to ensure the hypotensive ocular effect. Mannitol should be used with caution if the blood–aqueous barrier is not intact (anterior uveitis), because a leaky barrier may allow it to enter the vitreous, thereby pulling water into the vitreal cavity and increasing IOP. As mannitol expands the extracellular fluid volume, it has the potential to cause cardiac overload and dehydration in compromised patients, thus is contraindicated in patients with cardiac and renal disorders. With the introduction of PGAs, which are far more effective in decreasing the IOP, its use has become less common in the emergency treatment of acute congestive glaucoma. However, mannitol administration can be added to the protocol in severe refractory cases and in cases of secondary glaucoma due to primary anterior lens luxation where PGAs are contraindicated.

In secondary glaucoma, the underlying disease such as lens luxation or uveitis must be treated as a priority (see below).

An ophthalmologist should be consulted if the response to emergency medical treatment is not adequate, if surgery is recommended in an attempt to control the IOP, or if primary glaucoma is suspected, as long-term management will be required. In cases of unilateral primary glaucoma, the contralateral eye should receive prophylactic medication and regular pressure checks, and surgery (cyclodestructive procedure and filtering technique) should be recommended at the earliest indications of ocular hypertension. The owners should monitor for recurrence of pain, redness, pupil dilatation and blindness in the affected eye and for the appearance of any sign of glaucoma in the contralateral eye.

If the eye is irreversibly blind and the increasing IOP is refractory to medical or surgical treatment, enucleation or evisceration with intrascleral prosthesis is recommended in order to relieve the ocular pain and maintain the patient's quality of life.

Prognosis

Long-term prognosis for primary glaucoma depends on the length of time for which the medical and/or surgical treatment controls the IOP, but is usually poor. Recent improvements in techniques, materials, postoperative management, and patient selection have resulted in a better long-term outcome for surgical procedures. In the case of secondary glaucoma, the prognosis depends on whether prompt control of the underlying cause can be achieved. In cases in which the underlying cause can be found and addressed in a timely fashion (e.g. treatment of uveitis and surgical removal of lens luxation or instability) the prognosis for vision and/or the globe may be better than for primary glaucoma.

Acute uveitis

Definition

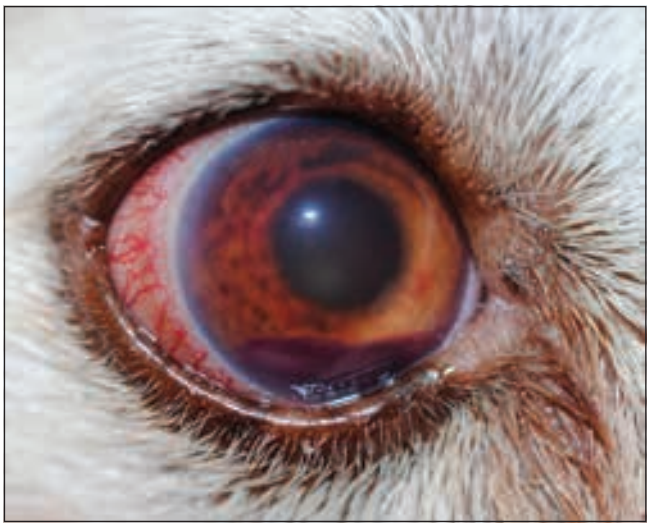
Uveitis is the inflammation of the uveal tract, which comprises the iris, ciliary body and choroid. Anterior uveitis is inflammation of the iris and ciliary body and posterior uveitis is inflammation of the choroid. Panuveitis is inflammation of all three portions of the uvea.

Acute uveitis is a painful condition, which requires urgent treatment to avoid the development of permanent structural lesions that may result in blinding consequences (e.g. secondary glaucoma, cataract, retinal detachment).

Clinical signs

Clinical signs of acute anterior uveitis include signs of ocular pain (blepharospasm, photophobia, tearing, enophthalmos), conjunctival hyperaemia, episcleral vascular injection, diffuse corneal oedema, aqueous flare, hypopyon, hyphaema, fibrin clots in the anterior chamber, miosis, and a swollen or dull appearance of the iris (Figure 10.23). If the posterior uvea is involved there may be vitreous haze or opacity, chorioretinal granulomas, retinal oedema, exudate, haemorrhage or detachment.

In anterior uveitis or panuveitis, the IOP is usually decreased (<10 mmHg) due to decreased aqueous humour production and increased uveoscleral flow mediated in



10.23 Acute anterior uveitis in a dog with lymphoma. The visible haziness in this eye is caused by slight corneal oedema and aqueous flare. Note the tearing, redness (due to conjunctival hyperaemia and episcleral vascular injection) and hyphaema.

part by prostaglandins. Increased IOP is occasionally observed in cases with severe uveitis and secondary glaucoma. Clinical signs of uveitis with normal IOP may signal early glaucoma development.

Diagnosis

The diagnosis of uveitis is based on clinical signs. Other common differential diagnoses for patients presenting with a red painful eye include glaucoma, corneal ulceration and scleritis. These diseases may not be mutually exclusive; for example, anterior uveitis can cause glaucoma, and corneal ulcers can cause neurogenic reflex anterior uveitis.

Uveitis can be associated with primary ocular disease (e.g. corneal ulceration, trauma, lens-induced uveitis, and primary neoplasia) or be secondary to a systemic infectious, immune-mediated (e.g. uveodermatological syndrome), metabolic, toxic or neoplastic cause, although there is inevitably considerable overlap on occasion. There are also occasions when the cause of the uveitis cannot be determined (idiopathic uveitis) (Figure 10.24).

Once uveitis is detected, every effort should be made to identify a specific cause of the inflammation so that the most effective treatment may be started. A thorough history and complete physical and ocular examinations are mandatory for the proper diagnosis of the cause of the inflammation. Diagnostic tests should be geared towards identification of the underlying cause and can include any of the following: complete blood cell count; serum biochemistry panel; coagulation panel; urinalysis; infectious disease screening (depending on geographical location); thoracic radiography; ocular and/or abdominal ultrasonography; and cytology/histopathology (e.g. lymph

Dog

- Trauma
- Lens-induced (phacolytic, phacoclastic uveitis or lens luxation)
- Ulcerative keratitis
- Scleritis (deep necrotizing or non-necrotizing)
- Neoplastic and paraneoplastic disorders:
  - Primary or secondary neoplasia (e.g. lymphoma, melanoma, carcinoma)
  - Histiocytic proliferative disease
  - Granulomatous meningoencephalitis (GME)
  - Hyperviscosity syndrome
- Infection:
  - Bacterial (septicemia of any cause, *Brucella canis*, *Leptospira* spp., *Borrelia burgdorferi, Bartonella vinsonii*)
  - Protozoal (*Toxoplasma gondii*, *Leishmania infantum*, *Neospora caninum*, *Trypanosoma evansi*)
  - Fungal (*Aspergillus fumigatus*, *Blastomyces dermatitidis*, *Candida albicans*, *Coccidioides immitis*, *Cryptococcus neoformans*, *Histoplasma capsulatum*)
  - Rickettsial diseases (*Ehrlichia canis*, *Anaplasma platys*, *Rickettsia rickettsia*)
  - Viral (adenovirus infection (including postvaccinal 'blue-eye'), canine distemper virus, canine herpesvirus)
  - Parasitic (*Cuterebra* spp., *Dirofilaria immitis*, *Angiostrongylus vasorum*, *Toxocara canis*, *Balisascaris* spp., *Onchocerca lupi*, *Encephalitozoon cuniculi*)
  - Algal (*Prototheca* spp.)
- Metabolic (e.g. systemic hypertension, coagulopathies, hyperlipidaemia)
- Immune-mediated disease (e.g. uveodermatological syndrome, immune-mediated thrombocytopenia, immune-mediated vasculitis)
- Pigmentary and cyst glaucoma in the Golden Retriever
- Toxaemia (e.g. pyometra)
- Drug-induced (particularly miotic and prostaglandin agents)
- Radiation therapy
- Idiopathic uveitis and exudative retinal detachment
- Idiopathic

Cat

- Trauma
- Primary or secondary neoplasia (e.g. lymphoma, diffuse iridal melanoma, sarcoma, carcinoma)
- Lens-induced (phacolytic, septic lens implantation syndrome or lens luxation)
- Ulcerative keratitis
- Infection:
  - Viral (feline leukaemia virus (FeLV), feline immunodeficiency virus (FIV), feline infectious peritonitis (FIP), feline herpesvirus-1).
  - Protozoal (*Toxoplasma gondii*, *Leishmania infantum*)
  - Bacterial (septicaemia, *Bartonella* spp.)
  - Fungal (*Blastomyces dermatitidis*, *Coccidioides immitis*, *Cryptococcus neoformans*, *Histoplasma capsulatum*)
  - Parasitic (*Cuterebra* spp., *Encephalitozoon cuniculi*)
- Metabolic (e.g. systemic hypertension, coagulopathies, hyperlipidaemia)
- Idiopathic (chronic lymphoplasmacytic)
- Periarteritis

10.24 Causes of uveitis.

nodes, skin, aqueous humour). For a detailed description of causes of uveitis and diagnostic approach, an ophthalmology text should be consulted (Maggs, 2017; Hendrix, 2013).

Treatment

Topical anti-inflammatory therapy should be instituted immediately after the diagnosis of anterior uveitis is made. Treatment with topical corticosteroids can be initiated in all cases of anterior uveitis pending the results of diagnostic tests, once a corneal ulcer has been ruled out with fluorescein.

Prednisolone acetate 1% or dexamethasone acetate 0.1% should be started and an initial application frequency of 3–6 times daily may be required.

Topical NSAIDs such as diclofenac, flurbiprofen, ketorolac, bromfenac, or nepafenac may be used q6–12h. They can be used either alone or in combination with corticosteroids since the therapeutic effect of using both is additive. Topical NSAIDs are commonly used to treat eyes with concurrent uveitis and corneal ulceration; however, patients with corneal ulceration should be monitored judiciously because an association between topical NSAIDs and corneal melting has been found in humans with infected ulcers.

Parasympatholytic drugs (atropine and tropicamide) improve the animal's comfort by paralysing the ciliary body (cycloplegia) and causing mydriasis, thereby minimizing the likehood of posterior synechiae formation (adhesions between the iris and anterior lens capsule). Atropine is the most effective ophthalmic parasympatholytic drug and also helps to decrease intraocular inflammation by blocking the effect of acetylcholine. Topical atropine sulphate may be applied q8–24h, as needed. If secondary glaucoma is present, atropine is contraindicated, with the rare exception of early iris bombé, which is defined as adhesions (synechiae) between the pupillary margin of the iris and the anterior lens capsule due to anterior uveitis. The condition results in the accumulation of aqueous humour in the posterior chamber, causing the iris to balloon forward blocking the drainage angle, which results in secondary glaucoma.

Tropicamide is a short-acting parasympatholytic drug that has a greater mydriatic effect than cycloplegic effect. It can be useful in treating cases of anterior uveitis in which IOP is borderline high.

If IOP is normal or elevated in the presence of inflammation, anti-glaucoma therapy may need to be started using a topical CAI (dorzolamide) alone or in association with a beta-blocker (timolol).

Systemic anti-inflammatory treatment with NSAIDs or steroids should be started in cases of severe anterior uveitis or posterior segment inflammation (posterior uveitis or panuveitis). Systemic corticosteroid therapy should not be initiated until diagnostic tests have been completed.

Treatment of the underlying cause, if found, is also necessary. This may involve specific treatment for infectious or neoplastic disease or immunosuppressive therapy if an immune-mediated disease (e.g. uveodermatological syndrome) is suspected. Lens-induced uveitis may require surgery (lensectomy) to decrease the inflammation and to maintain vision. In cases of uveitis with concurrent corneal ulceration, appropriate treatment with topical antibiotics is indicated. Annular posterior synechiae may cause complete obliteration of the pupillary opening leading to iris bombé and secondary glaucoma. Emergency surgery (synechiotomy) may be necessary in these cases.

Complications

Secondary complications include anterior or posterior synechiae formation, glaucoma, cataract, lens luxation, retinal detachment, retinal scarring and phthisis bulbi. Cases with a poor treatment response or cases involving multiple disease processes in the same eye should be referred to an ophthalmologist.

Prognosis

The prognosis depends on the underlying cause. Some systemic disease processes have a fair to good short-term prognosis for control of uveitis but a poor long-term prognosis for the animal (e.g. feline leukaemia virus/feline immunodeficiency virus (FeLV/FIV) infection). The prognosis can be good when the underlying cause can be controlled (e.g. sepsis, rickettsial or immune-mediated diseases) and prompt and adequate treatment is provided. The prognosis for traumatic uveitis depends on the extent of the corneal and intraocular damage.

Hyphaema

Definition and causes

Hyphaema is defined as the presence of blood in the anterior chamber. The most common causes are listed in Figure 10.25.

- Trauma
- Infection ± uveitis
- Neoplasia ± uveitis
- Immune-mediated ± uveitis
- Coagulopathy
- Congenital ocular diseases
- Systemic hypertension
- Chronic glaucoma
- Retinal detachment

10.25 Causes of hyphaema.

Clinical signs

The clinical signs are dependent on the primary cause. Additional systemic signs of a coagulopathy, trauma or medical causes of uveitis may also be present.

Diagnosis

Diagnosis is based on direct visualization of blood in the anterior chamber (see Figures 10.23 and 10.26). A thorough history and complete physical and ocular examinations are mandatory for the proper diagnosis of the cause of the hyphaema. When no history or other signs of trauma are found, the diagnostic plan should proceed as for uveitis. If a coagulation disorder is suspected, a full coagulation panel (platelet count, prothrombin time, partial thromboplastin time, and fibrin degradation products or D-dimers) should be submitted and a buccal mucosal bleeding time should also be performed. Systemic hypertension must be considered, especially in geriatric animals.

Extensive hyphaema prevents evaluation of the intraocular tissues and thus an ocular ultrasound examination should be performed in order to detect possible intraocular masses, vitreous haemorrhages, retinal detachment or scleral rupture. In cases of traumatic hyphaema,



10.26 Extensive hyphaema in a dog.

radiography or a computed tomography (CT) scan of the skull and orbit may be necessary to diagnose concurrent orbital fractures or foreign bodies.

Treatment

Treatment consists of treating the underlying cause if one is found. Treatment with topical corticosteroids can be initiated except in those cases with corneal ulceration. Prednisolone acetate 1% or dexamethasone acetate 0.1% should be started at an initial application frequency of 3–6 times daily. In cases of concurrent vitreous haemorrhage, systemic anti-inflammatory treatment with steroids or NSAIDs should be started, assuming no contraindications. Atropine sulphate 1% (one single dose or q12–24h) may also be used to reduce the possibility of posterior synechiae formation, decrease the ciliary spasm, and stabilize the blood–aqueous barrier. If secondary glaucoma is present, atropine is contraindicated with the rare exception of early iris bombé. Tropicamide can be used in cases in which IOP is borderline high. If IOP is elevated, anti-glaucoma therapy may need to be started as indicated for uveitis and secondary glaucoma. Tissue plasminogen activator (TPA) may be effective in the treatment of hyphaema when large blood clots and fibrin are present in the anterior chamber or the IOP is elevated secondary to fibrin blocking the aqueous drainage. These cases should be referred to an ophthalmologist for further evaluation and, if indicated, for intracameral TPA injection.

Complications

Common secondary complications include posterior synechiae, secondary glaucoma, cataract formation, corneal blood staining and phthisis bulbi.

Prognosis

The prognosis is variable depending on the underlying cause and the presence of secondary glaucoma or posterior segment damage. If bleeding can be controlled, the intraocular pressure is not increased and the posterior segment is not affected, the prognosis for vision can be good. If the haemorrhage is due to uveitis, the prognosis depends on the primary diagnosis.

Lens luxation

Clinical signs and diagnosis

Lens luxation can be diagnosed based on a change of lens position and the accompanying clinical signs. In anterior lens luxation, the lens can be visible in the anterior chamber (Figure 10.27) and signs of pain such as blepharospasm and tearing are usually present. Corneal oedema may be observed due to the physical contact between the lens capsule and corneal endothelium. In posterior lens luxation, the lens falls into the vitreous and an increase in the anterior chamber depth and iridodonesis (iris vibration) is usually seen. The posteriorly luxated lens sometimes gravitates to the ventral vitreous lying on the ventral retina.

Lens subluxation is a partial displacement of the lens and precedes lens luxation. In this case, vitreous fibrils floating through the pupil in the aqueous, iridodonesis, phacodonesis (lens movement) and an aphakic crescent (an area of the pupil where the lens is missing) may be seen.

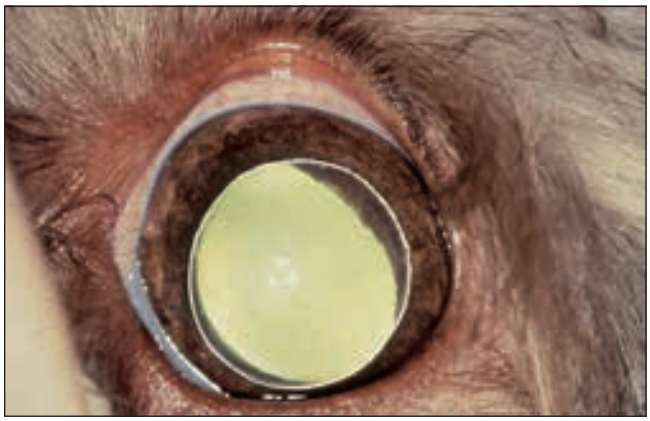
Lens luxation can be congenital, primary or secondary. Congenital lens luxation is a rare form of lens instability caused by the absence of zonular fibres attaching to the lens equator. Primary lens luxation involves an inherited zonular defect that in dogs results in lens instability manifesting at 3–6 years of age; breeds known to be predisposed include terriers, terrier crosses, Australian Cattle Dog, Border Collie, Brittany Spaniel, Chinese Crested Dog, Greyhound, Italian Greyhound, Lancashire Heeler, Petit Basset Griffon Vendéen, Pyrenean Sheepdog and Shar Pei. Because primary or inherent displacement is a bilateral disorder, although not necessarily with a symmetrical clinical presentation, the contralateral eye should also be evaluated, and will often reveal signs of lens instability, such as iridodonesis, phacodonesis, or an aphakic crescent. Secondary lens luxation can be caused by hypermature cataracts, chronic glaucoma, neoplasia and without concurrent ophthalmic disease in older dogs (senescence).

Feline lens luxation is most commonly secondary to uveitis and glaucoma. Primary lens luxation in cats is rare.

Anterior lens luxation or, less frequently lens subluxation, can be an emergency due to the high likelihood of secondary glaucoma. The IOP should therefore always be measured in these cases.

Treatment

In an emergency setting, if the IOP is increased a topical CAI can be started immediately. Mannitol (1–2 g/kg i.v. over 20–30 minutes) may also be administered if the response to the CAI is not adequate. Miotic anti-glaucoma drugs, such



10.27 Anterior lens luxation in a dog. The entire lens equator can be seen, and the lens partially covers the iris.

as PGAs (latanoprost, travoprost and bimatoprost), should not be used in cases of anterior lens luxation as they may potentiate pupillary block further worsening the glaucoma. The recommended treatment for anterior lens luxation is surgery and an ophthalmologist should be consulted as an emergency for further discussion regarding the risks and benefits of lens extraction in the affected eye, as well as a thorough evaluation of the risk of lens luxation in the contralateral eye.

If surgery is not an option, the lens can be 'pushed' back into the vitreous. One drop of a short-acting mydriatic (tropicamide) should be applied 15 minutes prior to the procedure. The lens is manipulated into the posterior chamber by digital pressure on the globe, a change of head position, or by rolling a sterile cotton- tipped applicator across the cornea, applying pressure and causing gentle depression of the corneal surface. A miotic agent (latanoprost, travoprost or bimatoprost) is then applied twice daily indefinitely to keep the lens in the vitreous chamber. This treatment is not ideal since the presence of the lens in the posterior segment may lead to retinal detachment and/or secondary glaucoma.

Prognosis

As lens luxation can lead to glaucoma, retinal detachment, uveitis and cataracts, the prognosis is guarded unless the lens luxation is diagnosed and treated early. With the numerous advances in surgical lens extraction over the last decade, the long-term prognosis has significantly improved. Secondary glaucoma and retinal detachment are the most common complications after lens extraction surgery.

Acute blindness

Causes

Blindness can be caused by lesions in four different locations and by different mechanisms: lesions that result in opacification of the clear ocular media (e.g. cataracts, severe uveitis, diffuse intraocular bleeding), lesions that cause failure of the retina to process the image (e.g. retinal detachment, retinal degeneration), lesions that impede transmission or relay of the message through the visual pathways (e.g. glaucoma, optic neuritis, chiasmatic tumours) and lesions that cause failure of the final processing of the image in the visual cortex (e.g. cerebral hypoxia after general anaesthesia). The most common causes of acute blindness are listed in Figure 10.28.

Acute blindness with ocular signs
• Uveitis • Intraocular bleeding • Glaucoma • Diabetic cataracts • Retinal detachment (e.g. bullous, rhegmatogenous, traction, dialysis) • Hypertensive retinopathy • Drug-induced retinal toxicity • Optic neuritis[a]
Acute blindness without ocular signs
• Sudden acquired retinal degeneration syndrome (SARDS) • Central nervous system disease (e.g. inflammation, infection, neoplasia, encephalopathy, head trauma, nutritional deficiency, toxicity, cerebrovascular accident, post-anaesthetic cortical blindness, after epileptic seizure)

10.28 Causes of acute blindness. [a] Ocular signs are present if the optic disc is affected (papillitis). In retro-bulbar optic neuritis without concurrent papillitis the funduscopy would be normal.

Diagnosis

A systematic clinical approach is required in cases of blindness. A thorough medical history and complete physical and ophthalmic examinations are the first steps. Visual tests such as the menace response cotton ball test, visual placement response and an obstacle course test may be performed to confirm blindness.

Lesions that produce opacification of the clear ocular media

These lesions may be easily detected during the ophthalmic examination. If there are signs consistent with uveitis or intraocular bleeding, the patient should be approached as previously described in this chapter (see above). Diabetic cataracts commonly develop rapidly and are bilateral. As they cause swelling of the lens and may produce spontaneous lens capsule rupture, severe phacoclastic uveitis and secondary glaucoma, the animal should be promptly referred for cataract surgery (phacoemulsification) if possible.

Lesions that cause failure of the retina to process the image

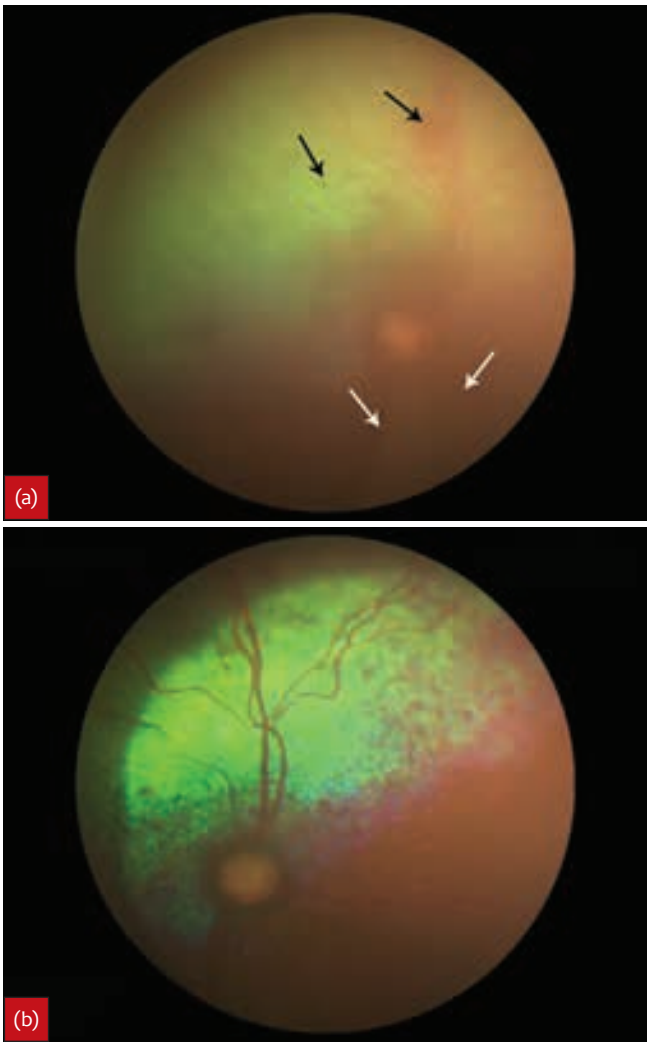
The majority of blind patients with retinal causes will have obvious abnormalities on ophthalmoscopy of both eyes and will have reduced to absent PLRs.

Retinal detachment may be identified on fundoscopic examination by an anterior displacement of the retinal surface and the retinal blood vessels. The detachment may be focal, multifocal, or complete. Generally, a small, focal retinal detachment will usually not result in clinically detectable impairment of vision, whereas significant detachment of the retina leads to appreciable vision deficits and blindness.

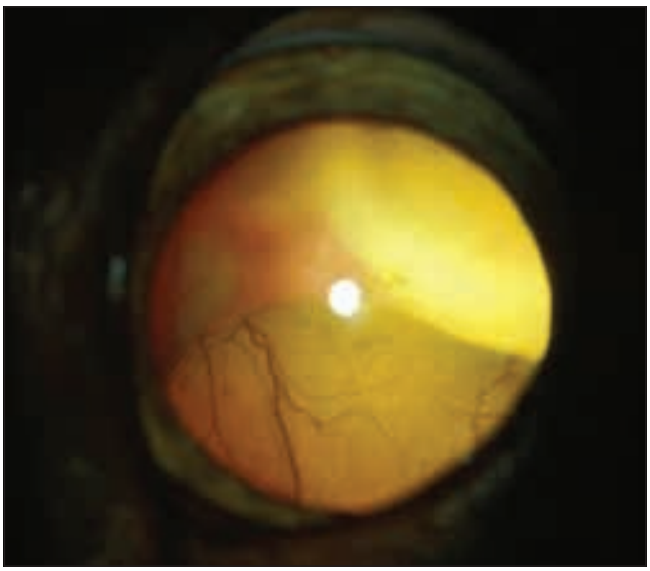
Retinal detachment can be subdivided according to the causative mechanism into:

- Bullous retinal detachment, when large volumes of subretinal fluid cause segments of the retina to balloon anteriorly (e.g. due to chorioretinitis or hypertension)
- Rhegmatogenous retinal detachment, when associated with a tear or hole in the retina, predisposing to leakage of vitreous beneath the retina and subsequent elevation (e.g. Collie eye anomaly, retinal and vitreal degeneration, lenticular diseases such as cataract and lens luxation, and after intraocular surgery)
- Traction retinal detachment, when associated with a vitreal disease where the vitreous pulls on the retina (e.g. from an organizing haemorrhage in the vitreous body)
- Dialysis, when there is complete tearing of the peripheral retina.

In cases of bullous retinal detachment the patient should be approached as for uveitis (see above). Hypertensive retinopathy secondary to systemic hypertension is a common cause of visual deficits in aged cats and less common in dogs. In both species acute blindness secondary to bullous retinal detachment is the most common reason for presentation. Clinical signs may include retinal arterial tortuosity, retinal and vitreal haemorrhage, retinal oedema, retinal detachment, hyphaema and secondary glaucoma (Figures 10.29 and 10.30). A non-invasive blood pressure measurement is used to confirm systemic hypertension.



10.29 (a) Fundoscopic image of a cat with blindness due to hypertensive retinopathy. Note the diffuse retinal oedema, multifocal retinal haemorrhages (black arrows), ventral retinal detachment (white arrows) and mild retinal vascular tortuosity. (b) The same eye 2 months after treatment with amlodipine. Note the substantial resolution of the retinal oedema, retinal haemorrhages and retinal detachment. The vision of this patient was recovered.



10.30 Bullous retinal detachment in a cat with systemic hypertension.
(Reproduced from Drobatz and Costello (2010) with permission from *Feline Emergency and Critical Care*)

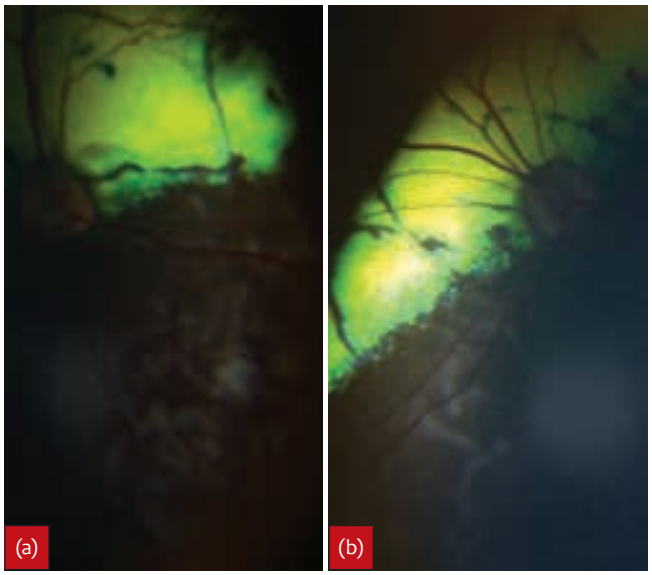
Management of hypertensive retinopathy includes controlling the underlying disease process (e.g. renal insufficiency, hyperthyroidism, hypothyroidism, hyperadrenocorticism, phaeochromocytoma, diabetes mellitus, primary aldosteronism) and treating the systemic hypertension with amlodipine, a calcium channel blocker (0.625–1.25 mg/cat q12h–24h orally; 0.05–0.4 mg/kg q12–24h orally in dogs; the dose may be increased slowly as required), or an angiotensin-converting enzyme inhibitor in dogs (benazepril HCl at 0.25–0.5 mg/kg q12–24h orally; enalapril maleate at 0.25–0.5 mg/kg q12h orally). Prognosis for vision depends on the length of time the retina has been detached. There is some evidence that the retina starts to degenerate within the first week of detachment (Anderson *et al*., 1986), so urgent treatment is mandatory.

Bilateral bullous retinal detachment for which an aetiology cannot be established despite laboratory work-up has been recognized in dogs and is termed steroid-responsive retinal detachment (Narfström and Peterson-Jones, 2013). Affected dogs typically present with a history of an acute-onset loss of vision. When a steroid-responsive retinal detachment is suspected, systemic steroids should be started as soon as possible after ruling out potential infectious and other systemic causes for which systemic steroids might be contraindicated. Treatment of retinal detachment depends on the presence of detectable underlying diseases and both the cause and the extent of the detached area. Even extensive bullous detachments may be re-attached with return of vision provided that appropriate medical treatment is initiated early. In cases of suspicion of rhegmetagenous retinal detachment, traction retinal detachment, or dialysis, an ophthalmologist should be consulted as an emergency for further discussion regarding the possibility of posterior segment surgery and retinal re-attachment.

Blindness induced by drug toxicity may be promptly discernible by the history (blindness usually appears within hours of administration or accidental ingestion). Ivermectin in dogs and cats and enrofloxacin in cats are well known retinotoxic compounds. In both cases, blindness is usually accompanied by mydriasis and clinical signs are bilaterally symmetrical. In cats affected by enrofloxacin retinal toxicity, fundoscopic examination reveals signs of retinal degeneration (tapetal hyperreflectivity and vessel attenuation) and the electroretinography (ERG) response is typically extinguished. In most cases, the blindness is permanent, although a few cases may retain some vision.

In cases of ivermectin toxicity, blindness may occur with or without marked central nervous system (CNS) signs (e.g. impaired level of consciousness, muscle tremors, ± hyper- or hypothermia, mydriasis ± positive PLRs, and various types of strabismus). Fundoscopic findings may include papilloedema and retinal oedema with folds (Figure 10.31). Blindness has also been observed with normal PLRs and a normal fundus. ERG may show absent or attenuated a and b waveforms. Visual loss is temporary, with recovery in 2–10 days.

In cases of sudden blindness with lack of significant ocular abnormalities, ERG is the gold standard diagnostic technique to distinguish between sudden acquired retinal degeneration syndrome (SARDS) and central causes of blindness. SARDS is a retinal disorder of unknown cause that results in sudden and permanent blindness in affected adult dogs due to loss of photoreceptor function. Most dogs show mydriasis, although some may retain PLRs. Typically, ocular fundus abnormalities are absent in the early stages. In SARDS, the electroretinogram is non-recordable, while with central causes of blindness, the



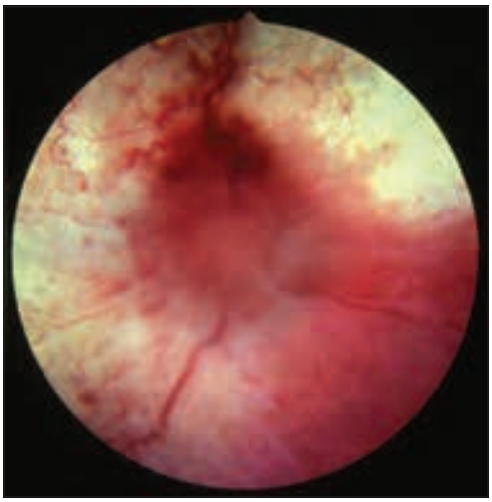
10.31 (a) Toxic neuroretinitis in a dog with acute blindness after accidental ingestion of ivermectin. Note the comma-shaped pigmentary changes in the tapetal fundus. In the non-tapetal fundus there are multiple areas of retinal oedema. (b)The dog recovered vision spontaneously 24 hours after presentation.

electroretinogram is relatively normal. The disease typically affects middle-aged to elderly and often moderately overweight dogs. Between 60 and 90% of affected dogs are female and the majority of them are neutered. Most dogs with SARDS also have systemic signs and altered clinicopathological test results suggestive of hyperadrenocorticism, such as polyuria, polydipsia, polyphagia, weight gain, lymphopenia, lymphopenia with neutrophilia, elevated alkaline phosphatase and hypercholesterolaemia. Some cases may be confirmed as having hyperadrenocorticism. There is currently no widely accepted treatment for SARDS. In the subset of dogs diagnosed concurrently with hyperadrenocorticism, appropriate therapy for this condition is suggested.

Lesions that impede transmission or relay of the message through the visual pathways

In glaucoma, the increased IOP impairs blood flow and axoplasmic flow of the optic nerve, which leads to a cascade of biochemical changes that induces retinal ganglion cell dysfunction, resulting in optic nerve degeneration and atrophy, visual field loss and blindness. If there are clinical signs consistent with glaucoma the patient should be approached as previously described in this chapter.

Clinical signs of bilateral optic neuritis are acute blindness with fixed and dilated pupils. Optic neuritis may be detected by ophthalmoscopy (if the optic disc is affected; termed papillitis), and usually appears as a swollen, oedematous and hyperaemic optic nerve head (Figure 10.32). If the retrobulbar optic nerve is affected without concurrent papillitis, the fundic examination would be normal. In this situation, ERG is required to distinguish between SARDS and retrobulbar optic neuritis. ERG results should be normal in a patient affected by optic neuritis. Causes of optic neuritis in dogs are infection (blastomycosis, cryptococcosis, histoplasmosis, toxoplasmosis, neosporosis, distemper, ehrlichiosis and canine tick-borne encephalitis virus), inflammation (granulomatous meningoencephalitis (GME)) and necrotizing meningoencephalitis (NME)), trauma, toxicity, orbital abscess/cellulitis, optic nerve and orbital neoplasia, and idiopathic. Optic neuritis



10.32 Severe optic neuritis in a cat with cryptococcosis. The optic nerve head appears swollen, oedematous, congestive, and with blurred margins. Several retinal and optic nerve haemorrhages are also present.
(Courtesy of C Peruccio)

appears to be less common in cats than in dogs. Causes for optic neuritis in cats are infection (feline infectious peritonitis (FIP), toxoplasmosis, and cryptococcosis), trauma, orbital abscess/cellulitis, and optic nerve and orbital neoplasia.

In cases of optic neuritis or suspicion of any other central nervous system disease, a complete neurological examination, routine laboratory investigations, cerebrospinal fluid analysis and magnetic resonance imaging are necessary to confirm the exact location of the lesion, to reach a prompt diagnosis and to determine the most appropriate treatment.

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Chapter 11

Approach to gastrointestinal emergencies

Gareth Buckley and Elizabeth Rozanski

An 'acute abdomen' is defined as sudden abdominal pain or signs of gastrointestinal upset of an unidentified cause. Any patient presenting with signs of abdominal distress should be promptly evaluated, with the primary goals of the initial examination being to assess cardiovascular stability, assess for the possibility of surgical disease, and if possible, to localize the problem based on physical examination.

Abdominal signs may be caused by surgical or non-surgical gastrointestinal disease, or by extra-gastrointestinal disease, such as hepatic, pancreatic, urogenital, splenic, endocrine (e.g. diabetic ketoacidosis) or even musculoskeletal disease. Dogs with pericardial effusion commonly vomit 24–48 hours prior to presentation with signs of cardio-vascular collapse. Some clinicians consider pancreatitis or hepatic disease as an extension of gastrointestinal disease, while others consider them a separate entity.

Many animals with acute gastrointestinal signs will respond rapidly to supportive care, often without a specific diagnosis being made. The purpose of this chapter is to review the diagnostic and therapeutic approach to the assessment of the patient presenting with acute abdominal signs.

Initial assessment

The initial assessment of the dog or cat presented for abdominal pain and/or vomiting and diarrhoea should include an assessment of the stability of the major body systems, i.e. the heart, brain and lungs. Specifically, dogs should be assessed for signs of shock (most commonly hypovolaemic or distributive), including tachycardia (>160 bpm), weak pulses and changes in mucous membrane colour or capillary refill time as well as fever, laboured respiration or dull mentation. If shock is present, or thought to be present, it should be promptly assessed and treated (see Chapter 3). Abdominal pain should be assessed, and if possible localized. In chondrodystrophic dogs, such as Dachshunds, back pain masquerading as abdominal pain should be excluded. Animals with hypovolaemia due to excessive vomiting or diarrhoea are typically treated with intravenous crystalloid boluses (20–30 ml/kg repeated to effect; see Chapter 4). Patients with active haemorrhage require special consideration; this is discussed in Chapters 4 and 12.

Cats are often harder to assess, but a similar evaluation for shock to that of dogs should be undertaken; cats with hypothermia and bradycardia are often hypovolaemic. Additionally, in male cats, urethral obstruction should be excluded – this is usually straightforward based on abdominal palpation. Patients with aortic thromboembolism ('saddle thrombus') may present with severe pain, but it is generally simple to identify on physical examination due to the lack of femoral pulses (see Chapter 6).

If patients are perceived to be unstable, prompt therapy should be initiated to improve the patient's cardiovascular status, including administration of intravenous fluid boluses as well as antibiotics if indicated, and possibly analgesics if pain is a significant component. In stable patients, a more complete physical examination and history taking may be completed prior to further diagnostic tests or treatment.

Other important historical considerations include the age, sex and breed of the patient, as well as any past pertinent history, with a specific focus on gastrointestinal signs. Some dogs may be prone to ingestion of foreign bodies even as they mature. Vaccination and worming status and/or exposure to other potentially infectious dogs should be investigated. Normal diet, including routine exposure to raw meats, should be evaluated as well as any potential dietary indiscretions such as eating from the bin, recent changes in diet or consumption of high-fat foods.

The duration and progression of clinical signs should be reviewed, as well as any home therapies. For vomiting patients, pertinent questions include confirmation of whether the animal is vomiting rather than regurgitating (i.e. active abdominal component or not), and establishment of any potential useful characteristics of the vomitus, such as the presence of blood, bile or foreign objects. For animals with diarrhoea, useful questions include the presence of urgency, straining, or bloody, mucoid or melaenic faeces, with the aim being to differentiate between small and large bowel diarrhoea.

Small bowel diarrhoea is characterized by only a slight increase in frequency of defecation but a high volume of stool per defecation. Conversely, patients with large bowel diarrhoea typically have a significant increase in frequency of defecation with straining and only small amounts of stool with mucus and occasionally fresh blood produced each time.

Following a complete history and physical examination, a recommendation should be made to the client regarding further diagnostics or therapy. In animals with a reassuring physical examination and uncomplicated history, simple supportive care may be adequate, such as an antiemetic and a bland diet. However, in many cases, further diagnostics and therapies are indicated.

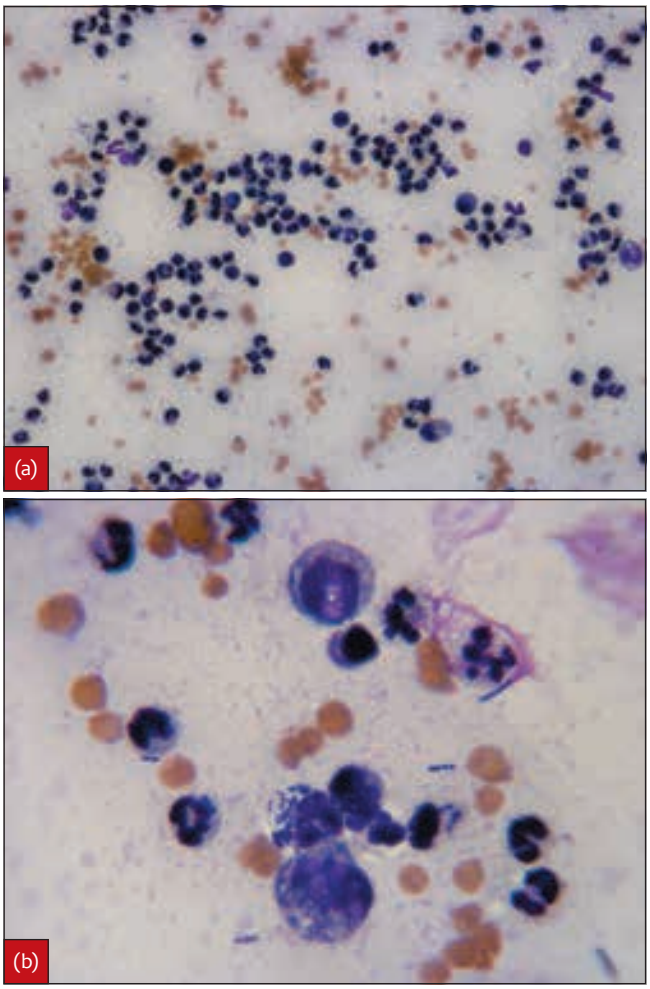
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Diagnostic testing

Diagnostic testing includes imaging and laboratory testing; the focus is on ruling in or out surgical disease or extra-gastrointestinal causes of acute abdominal signs such as diabetic ketoacidosis and acute kidney failure. The extent and choice of diagnostic testing is usually decided by history and physical examination, as well as the owners' wishes and the finances available. For example, abdominal imaging, typically radiography as a first line, should be recommended in a dog known to ingest foreign bodies which has some mild abdominal pain; however, symptomatic treatment is often appropriate for a dog with mild vomiting and diarrhoea, with no suspicious history, that has an otherwise unremarkable physical examination. If suspicion exists for gastric dilatation–volvulus, e.g. distended or very painful abdomen, then imaging is mandatory to confirm the diagnosis. Additionally, if oesophageal foreign body is a differential (e.g. animal with regurgitation, increased swallowing) then imaging (thoracic radiography) should be performed, as this condition is impossible to rule in or out on physical examination. A more extensive workup including bloodwork and detailed imaging such as abdominal ultrasonography is indicated in animals demonstrating signs of systemic inflammatory response (fever (or hypothermia in cats), cardiovascular instability, tachypnoea or significant alterations in white blood cell count), or in patients where conservative management has failed. Ultrasonography is more effective than radiography for imaging the abdomen when significant effusion is present, such as seen in ascites from hypoalbuminaemia or liver disease, septic peritonitis, haemoabdomen or severe pancreatitis. Ultrasonography is very operator dependent but can also be significantly more sensitive and specific for the diagnosis of intestinal obstruction than radiography alone, although the combination of the two modalities can be extremely helpful. In general, imaging is low yield in animals with acute diarrhoea as the main presenting complaint; in these animals, bloodwork and faecal examination are likely to be more helpful in reaching a diagnosis.

Imaging

In many emergency rooms, abdominal focused assessment with sonography for trauma (FAST) has emerged as an indispensible tool. Focused ultrasonography is useful for detecting free fluid, which may be promptly sampled, and subsequently evaluated to establish a diagnosis of haemorrhage, sepsis, neoplasia or urinary or biliary tract rupture. Haemorrhage is identified by gross inspection of the fluid, as well as determination of the spun haematocrit of the fluid. Additionally, blood from spontaneous haemoperitoneum will not clot; if the blood clots then it is likely that an organ such as the spleen has been aspirated. Sepsis may be confirmed by the microscopic identification of intracellular bacteria within neutrophils (Figure 11.1). A septic effusion is suspected if the abdominal effusion glucose is lower than the peripheral blood glucose by 1.1 mmol/l or more or the abdominal effusion lactate is greater than peripheral blood lactate by 2.0 mmol/l or more (Bonczynski *et al*., 2003) (this test may be less accurate in cats (Levin *et al*., 2004)). Neoplasia may be confirmed by the presence of neoplastic cells in the effusion, although it is important to recognize that reactive mesothelial cells may be difficult to distinguish from neoplastic cells and the absence of neoplastic cells does not exclude cancer. Urinary tract rupture should be suspected in the presence



11.1 Microscopic images of a septic peritoneal effusion in a dog. (a) X40 lens. (b) X100 oil immersion lens.
(Courtesy of K Papasouliotis)

of elevated creatinine and potassium in relation to the peripheral blood (Schiedt *et al*., 2001) and confirmed by a contrast study or exploratory surgery. Typically, in dogs an effusion:blood ratio of 2:1 for creatinine or 1.4:1 for potassium is considered diagnostic for uroabdomen, although any increase in effusion concentration of potassium or creatinine compared with peripheral blood is highly suggestive. In cats, a ratio for creatinine of 2:1 and for potassium 1.9:1 is considered diagnostic (Aumann *et al*., 1998). A more detailed discussion of these conditions and their management can be found in Chapters 8 and 12.

Diagnostic peritoneal lavage (DPL) is occasionally referred to in older literature as a technique to retrieve abdominal effusion for diagnostic testing. Focused ultrasonography has largely replaced DPL, although it remains of historical interest and may be performed if ultrasonography is not promptly available or if a very small amount of fluid can be identified on ultrasonography that cannot be tapped directly (Figure 11.2).

Abdominal radiography is a useful diagnostic modality for evaluating the intra-abdominal structures in dogs and cats with signs of acute abdominal disease. The abdominal structures should be evaluated in a systematic fashion, with a focus on the gastrointestinal tract, as well as the size and shape of the liver, kidneys, urinary bladder and reproductive tract (see Chapter 24). Identification of intestinal gas patterns consistent with obstruction, mass or mass-effect, or free intra-abdominal air should prompt surgical exploration. In cases where gas patterns are

Diagnostic peritoneal lavage is performed to retrieve cells from the abdomen when only a tiny volume of fluid is present precluding direct centesis.

1. The animal is placed in lateral recumbency and the bladder emptied. The abdomen is clipped and prepared as for a sterile surgical procedure. Sedation is rarely required but can be used if necessary.
2. A fenestrated, over-the-needle catheter (minimum 18 G) is inserted caudal to and to the left of the umbilicus and directed cranially. Once the peritoneal cavity is penetrated, the catheter is slid off the stylet and the stylet is removed. A local block with 2% lidocaine can help with patient compliance.
3. Through this catheter, 10–20 ml/kg of warmed (body temperature) 0.9% saline is infused over several minutes. Infusion can be achieved by gravity flow or by injection with very gentle pressure.
4. Once the fluid has been infused, the catheter is removed and the animal is either gently rolled or walked around to disperse the fluid throughout the peritoneal cavity.
5. Standard abdominocentesis (right cranial quadrant) is then performed to obtain a representative sample for analysis.

It is unusual to recover more than a few millilitres of the infused fluid; this should be taken into account when considering ongoing fluid therapy in these patients.

11.2 Technique for performing diagnostic peritoneal lavage.

suspicious but not completely diagnostic for obstruction, repeat radiography 6–12 hours later can help the clinician to assess whether the gas pattern is changing, worsening or resolving. This may also be helpful in assessing whether foreign material is moving through the intestines and is likely to be passed or whether it appears obstructive. In skilled hands, abdominal ultrasonography is also a helpful adjunct in these cases. Abdominal radiography is a useful screening tool for non-surgical disease; loss of abdominal detail may indicate the presence of abdominal effusion, which should lead to either blind or ultrasound-guided abdominocentesis. Loss of detail in the right cranial quadrant of the abdomen is consistent with pancreatitis, although certainly not definitive. Generalized distension of the intestines is indicative of a functional ileus.

If abdominal radiography and focused ultrasonography do not identify a clear cause of the acute abdominal signs, a complete abdominal ultrasound examination may be performed. Some clinicians elect to bypass abdominal radiography in favour of a complete abdominal ultrasound examination; the utility of this approach depends on the skills of the ultrasonographer and the patient assessment by the clinician. Ultrasonography in skilled hands can be extremely useful for assessing for pancreatitis, lesions in the liver such as masses or abscesses, focal changes to the intestines such as changes in wall layering, masses or obstructions. If small volumes of peritoneal fluid are present, then ultrasound guidance can be invaluable in obtaining samples for analysis.

Other forms of abdominal imaging, including computed tomography (CT) or magnetic resonance imaging, are uncommonly performed in veterinary medicine at this time, especially in the emergency and critical care setting. Some diagnostic imaging specialists favour abdominal CT scanning for larger dogs in place of abdominal ultrasonography, especially in deep-chested or uncooperative dogs.

Laboratory analysis

Laboratory testing is also indicated in dogs and cats with acute abdominal signs and may include point-of-care testing, as well as more specialized testing. Point-of-care testing includes determination of the spun haematocrit and total protein, determination of blood glucose and lactate, blood smear evaluation, electrolyte and acid–base assessment, and coagulation testing if indicated. Haemoconcentration will be reflected by an increased spun haematocrit, sometimes in excess of 60%. Dehydrated patients may also have an elevated total protein, often greater than 80 g/l, although with simultaneous haemorrhage or a protein-losing enteropathy the total protein may be within the reference range or even decreased. Dogs with haemorrhagic gastroenteritis usually present with a high haematocrit and low total protein due to loss of the plasma component of blood into the intestinal tract. In some cases of diabetic ketoacidosis the presenting complaint is vomiting and weakness; in these cases the blood glucose is typically severely elevated, usually in excess of 17 mmol/l and often greater than 33 mmol/l.

Electrolyte and acid–base screening is often performed early in the evaluation of animals with acute abdominal disease and can assist the clinician with diagnosis, treatment and monitoring (see Chapter 5). Certain classic electrolyte disturbances can quickly point the clinician to a likely diagnosis; for example, severe hyperkalaemia with concurrent hyponatraemia in a vomiting dog would prompt testing and treatment for Addison's disease. High intestinal or pyloric obstruction would be suspected in a young vomiting dog with severe metabolic alkalosis. In any case, severe electrolyte disturbances should be addressed early in the course of treatment regardless of the cause. In animals which are bleeding or anaemic, blood smear evaluation especially to assess platelet count can be a useful early test, as can coagulation testing such as activated clotting time (ACT) or prothrombin/partial thromboplastin time (PT/PTT), all of which are now available as bedside tests. A finding of severe coagulopathy would prompt a search for a cause (for example anticoagulant rodenticide intoxication, certain heparin secreting tumours, disseminated intravascular coagulation) and could prompt early therapy with plasma transfusion to replenish clotting factors (see Chapter 15).

Other laboratory testing that may be pursued include a complete blood count, biochemical profile, and urinalysis, as well as more focused testing such as pancreatic lipase immunogenicity or adrenocorticotropic hormone (ACTH) stimulation tests. Laboratory testing in animals with acute abdominal signs is performed to evaluate the patients for extra-gastrointestinal causes of abdominal signs, as well as to evaluate for any comorbidities that might complicate care, such as severe electrolyte disturbances, azotaemia, liver dysfunction, or leukocyte abnormalities, such as a degenerative left shift.

Azotaemia may be pre-renal, renal or post-renal in origin. Evidence of inadequate urine concentration (urine specific gravity <1.030) is often taken as a confirmation of renal azotaemia; however, it is prudent to recall that therapies such as prednisolone or furosemide and some medical conditions such as hyperadrenocorticism and hypercalcaemia may impact the concentrating ability of the kidneys. Severe kidney or liver disease often presents with anorexia or vomiting as the initial complaint and in some cases acute kidney injury or acute hepatic necrosis can be markedly painful.

Supportive care

Fluid therapy

Fluid therapy represents the cornerstone of supportive care for patients with acute abdominal disease. Large volumes of fluid and electrolytes are secreted and

reabsorbed by the healthy gastrointestinal tract daily. In a 20 kg dog approximately 2.5 l of fluid enters the gastrointestinal tract from diet and normal gastrointestinal secretions and over 98% is reabsorbed daily. Of the fluid entering the gastrointestinal tract, approximately one-quarter to one-third is from external sources (food and water) and the majority is from endogenous secretions (salivary glands, stomach, small intestine, liver and pancreas). The nature of the fluid secreted at different points along the gastrointestinal tract is quite variable and so the systemic derangements also vary depending on the exact nature of the disease. When treating a patient with fluids, important concepts to be considered include patient characteristics, underlying disease, hospital or clinic characteristics, and fluid types and volumes (see Chapter 4).

Normal fluid balance is based upon adequate food and water intake. Reported 'maintenance' fluid rates for healthy animals are 40–80 ml/kg/day; however, this can vary widely depending on the size of the patient. As a guideline, 2–3 ml/kg/h is a reasonable intravenous fluid rate in a patient that is adequately hydrated, but not able to maintain hydration for any reason, e.g. vomiting. Animals with excessive fluid losses, including polyuria/polydipsia, vomiting/diarrhoea, panting or wound/body cavity exudate, will require even higher levels of fluid support to make up for ongoing losses and prevent development of dehydration and/or hypovolaemia.

For animals with acute abdominal signs, it is essential to determine if the patient is hypovolaemic, simply dehydrated or both (see Chapters 3 and 4 for more information). Hypovolaemia with normal interstitial hydration is typically seen in animals with peracute onset of abdominal disease, such as those with gastric dilatation–volvulus, where, despite the presence of intravascular volume depletion, the interstitium at first is adequately hydrated due to the limited duration of clinical signs. Clinical signs of hypovolaemia include tachycardia, pale mucous membranes, weak pulses, quiet mentation and occasionally tachypnoea. Biochemically, shock is appreciated by increased lactate (>3.0 mmol/l) and increased base deficit. These patients should be promptly treated for shock, with an initial intravenous fluid bolus of 20–30 ml/kg of isotonic crystalloids; this bolus can be repeated following reassessment until the cardiovascular parameters improve.

In animals with simple dehydration, the cardiovascular parameters remain normal, but the patient has evidence of fluid loss. Dehydration is appreciated clinically by dry mucous membranes (if the animal is not panting or salivating heavily), decreased skin turgor, and progressively by sunken eyes followed by tachycardia and collapse as dehydration progresses to hypovolaemia. Skin turgor in older cats in particular can be misleading, as they often feel dehydrated even when normal, and young puppies may have good skin turgor despite having marked dehydration. A dehydrated animal that is also hypovolaemic should be treated for hypovolaemia first, and then have the dehydration corrected over several hours (see Chapter 4). It may be challenging to estimate the percentage of dehydration without knowledge of prior bodyweight, although charts (Figure 11.3) are popular and may give a reasonable starting point.

In treating dehydration, the goal is to replace the fluid deficit, provide maintenance needs, and to support any potential ongoing losses. Estimating the percentage dehydration is helpful in determining a fluid rate, so while there are inherent flaws in doing so, it is helpful clinically to pick a number, such as 8%, using the parameters outlined in Figure 11.3. The crystalloid dose is calculated by multiplying the weight in kilograms by the percentage dehydration. For example, a 20 kg dog that is assessed to be 8% dehydrated would require 20 x 0.08 = 1.6 kg (or 1600 ml) of fluids for rehydration. Importantly, fluid therapy should also provide for ongoing losses as well as normal maintenance needs in order to prevent recurrence of dehydration. In this case, a 20 kg dog would need a normal maintenance fluid rate of approximately 60 ml/kg/day (or 1200 ml), and might require an additional 400 ml to replace ongoing excessive losses (e.g. diarrhoea). This patient would then receive 3200 ml of fluid per day (1600 ml dehydration + 1200 ml main-tenance + 400 ml ongoing losses) or a total of 133 ml/h. Practically, the clinician might set the fluid rate at 130 or 150 ml/h.

Percentage dehydration	Clinical signs
<5%	No signs on physical examination, but historical finding consistent with a volume loss
5%	Dry mucous membranes (in the absence of panting)
7–8%	Dry mucous membranes, decreased skin turgor ± slight tachycardia caused by early hypovolaemia
10–12%	Dry mucous membranes, decreased skin turgor, mild to moderate tachycardia and weak pulses caused by moderate hypovolaemia
>12%	All of the above and progression to severe hypovolaemia, shock and collapse

11.3 Physical examination parameters used to estimate percentage dehydration in dogs.

Types of fluids

Fluids can be crystalloids or colloids. Crystalloids consist of electrolytes in water and are freely diffusible across the vascular space. These include replacement fluids, which are fluids with a sodium concentration similar to that of plasma (e.g. sodium 130–154 mmol/l) and are the fluid type most commonly used in veterinary medicine. Examples of crystalloid replacement fluids include 0.9% saline, Hartmann's solution, lactated Ringer's solution, and other balanced electrolyte replacement solutions (e.g. Plasmalyte 148 and Normosol-R in USA). Crystalloids may also be maintenance fluids, with lower sodium levels (e.g. 0.45% saline, and Plasmalyte 56 or Normosol-M in the USA). These fluids have sodium concentrations that are about half of those in plasma, and are used for animals which are hydrated, but are expected to have ongoing fluid needs because of a lack of intake. Fluids typically used in practice are almost always replacement fluids, but occasionally fluid therapy is referred to in multiples of maintenance (e.g. 3 x maintenance). While beyond the scope of this chapter, parenteral nutrition products (e.g. Procalamine, peripheral (PPN) and total (TPN) parenteral nutrition) are also crystalloids. Opinions vary about whether the volume of parenteral nutrition products should be included as part of the fluid calculations; this is of particular concern in patients with evidence of heart disease or volume overload. Crystalloids leave the vasculature and equilibrate with the extravascular space quickly when given intravenously, and are absorbed quickly when given subcutaneously.

Colloids are fluids that contain water, electrolytes and large molecules that do not easily move out of the vascular space. Colloids can be natural, such as whole blood or

plasma, or concentrated albumin, or may be synthetic, such as hetastarch or tetrastarch. Synthetic colloids are sometimes considered in patients with gastrointestinal disease, particularly if they have low total protein levels; however, the rationale for their use and the risk:benefit should be carefully considered. For example, if the patient has had chronic gastrointestinal protein loss, interstitial protein levels may also be depleted, meaning the osmotic gradient between the vasculature and the interstitium may not be significantly affected. In this scenario, the rationale of using colloids to increase oncotic pressure and reduce the risk of oedema development may not be necessary. Furthermore, there are increasing concerns over the possible adverse effects of colloids, and whilst these concerns have not been as well documented in small animals as in humans, evidence is emerging that similar effects are seen. Natural colloids such as plasma or albumin may be used as clinically indicated; however, it is essential to recall that fluid rates are not interchangeable between crystalloids and colloids (see Chapter 4 for a more detailed discussion of fluid therapy).

Fluid additives

Electrolyte and metabolic disturbances are common in animals with gastrointestinal disease and in animals being treated with fluid therapy; fluid additives such as potassium or dextrose supplementation may be used to correct these. Potassium should not be added to fluids that are being administered as a bolus, as too rapid an infusion of potassium will result in cardiac arrhythmias or cardiac arrest. Potassium may be added to fluids being given for rehydration, and should be added at a rate to correct hypokalaemia as needed. The usual maximum rate of infusion of potassium is 0.5 mmol/kg/h in order to avoid bradyarrhythmias. Most animals do not require this level of supplementation for more than 4–6 hours, and if it is continued, serum potassium concentrations must be monitored at least twice daily and ideally every 4–6 hours. In small animals on high fluid rates the maximum rate of potassium infusion may be easily reached; for example, in a cat weighing 4 kg, if the desired fluid rate was 40 ml/h, the maximum amount of potassium to add per litre would be 50 mmol; conversely, if the desired fluid rate was only 10 ml/h, up to 200 mmol/l of potassium chloride could be added to the crystalloids for infusion.

Dextrose infusions should be given only to patients with documented hypoglycaemia, typically less than 3.6 mmol/l, while at the same time the patient is evaluated for the cause of the hypoglycaemia. Supplementing a patient with low normal glucose (e.g. 4.2 mmol/l) may not be beneficial, as this can result in increased secretion of insulin and may cause a further decline in circulating glucose levels.

Adjusting fluid therapy

Following rehydration, fluid therapy should be tapered to support ongoing needs. Food and water may be slowly introduced; bland food is commonly recommended in small quantities as tolerated. Most gastrointestinal disturbances resolve quickly and the patient may be transitioned back to their routine diet and discharged home. Following non-specific supportive care, failure to improve in a timely fashion should prompt clinical re-investigation for the cause of the problem, allowing institution of specific treatment as required.

Medical therapy

Medications are often used in conjunction with fluid therapy for patients with acute medical abdominal disease. A list of commonly prescribed groups of medications with details of individual drugs and suggested doses is given in Figure 11.4. Use of these medications for specific conditions will be discussed in the next section. Note that these are recommendations based on personal experience; clinicians will need to follow local drug licensing and prescribing rules, which vary from country to country.

Class	Drug	Dose	Route	Dosing interval	Notes
Antiemetics	Maropitant	1 mg/kg	s.c.	q24h	5 day maximum treatment time in Europe
		2 mg/kg	Orally	q24h	
	Metaclopramide	1–2 mg/kg/day	i.v.	Constant rate infusion	Also has a prokinetic effect on the stomach
		0.2–0.5 mg/kg	s.c., orally	q6–8h	
	Ondansetron	0.2–0.5 mg/kg	i.v., orally	q8–12h	
	Erythromycin	1–2 mg/kg	Orally, i.v.	q8–12h	Intestinal promotility agent
H2 antagonists	Famotidine	0.5–1 mg/kg	i.v., s.c., orally	q12–24h	
	Ranitidine	0.5–2 mg/kg	i.v., orally	q12h	May have prokinetic effect, limited efficacy for changing gastric pH
	Cimetidine	10 mg/kg	Orally	q6h	Short half-life, limited efficacy for changing gastric pH
Proton pump inhibitors	Omeprazole	1 mg/kg	Orally	q12h	Dosing q24h may be useful for maintainance therapy; however, q12h dosing recommended for acute gastric ulcer disease
	Pantoprazole	0.6–1 mg/kg	i.v.	q12h	
	Lansoprazole	0.5–1 mg/kg	Orally	q12h	
Other anti-ulcer	Sucralfate	0.5–1 g	Orally	q6–8h	Can dissolve tablets or use liquid suspension
Anti-infectives	Metronidazole	10–15 mg/kg	i.v., orally	q12h	Higher dose often used for *Giardia* but risk of developing vestibular signs at >30 mg/kg/day
	Fenbendazole	50 mg/kg	Orally	q24h	For most intestinal parasites, treat for 3 days then repeat in 3 weeks

11.4 Drugs commonly used in the treatment of gastrointestinal disease.

Antiemetics

These medications act at various sites both locally in the intestine and centrally in the central nervous system. When choosing an antiemetic medication, thought should be given to the route and ease of administration as well as what is trying to be achieved. For example, an animal with ongoing regurgitation and gastric ileus will likely benefit more from a prokinetic agent such as metoclopramide than from a centrally acting anti-nausea drug such as ondansetron. A patient with severe small intestinal ileus will likely benefit from erythromycin more than metoclopramide, as metoclopramide has no effect on small intestinal motility. For general vomiting/nausea both maropitant and ondansetron and related drugs will work effectively. In severe cases they can also be combined either with each other or with promotility agents such as metoclopramide.

H2 antagonists

This class of drugs act to increase gastric pH and make it more likely that ulcers will heal, or to prevent peptic ulcer formation. Unfortunately, there is limited evidence that these drugs are effective at increasing gastric pH to levels that would encourage ulcer healing. Famotidine appears to be the most effective, especially at high doses; however, ranitidine and cimetidine are still widely used and may have other beneficial effects, such as the promotility effect seen with ranitidine.

Proton pump inhibitors

This class of drugs act at the proton pump and are potent inhibitors of gastric acid secretion. They are generally more effective than the H2 antagonists at increasing gastric pH, especially when used at a high dose or when used twice daily. Therapeutic effects persist for several days after cessation of therapy.

Others

Sucralfate is used as a suspension to coat ulcers and allow them to heal. It can also provide some degree of relief from oesophageal ulceration caused by acid reflux. It acts best in an acidic environment, so should ideally be given prior to antacids. Sucralfate can interfere with absorption of other medications, so separation of dosing of sucralfate from other oral drugs seems prudent.

Anti-infectives

Most commonly, antimicrobial drugs are used to treat *Giardia* (metronidazole and fenbendazole) or intestinal worms (fenbendazole). Metronidazole is commonly used in cases of colitis and bloody diarrhoea; while the use for this indication remains widespread, its use is controversial and there is little evidence for its efficacy. Other antimicrobial drugs are rarely used in the acutely unwell patient; however, there are exceptions – see Specific diseases (below) for a more detailed discussion.

Specific diseases

Haemorrhagic gastroenteritis

Haemorrhagic gastroenteritis is a syndrome of bloody vomiting and diarrhoea, often peracute in onset (Figure 11.5). Small-breed dogs are over-represented and severe



11.5 Typical appearance of severe haemorrhagic gastroenteritis.

haemoconcentration (packed cell volume (PCV) 70–75%) at the time of presentation is common. Due to loss of plasma proteins into the gastrointestinal tract, this is often accompanied by a low total protein (<60 g/l). Laboratory analysis is typically unremarkable except for these changes to proteins and PCV. Lactate may be elevated due to hypovolaemic shock. Abdominal imaging typically shows gas- and fluid-filled intestines without an obstructive pattern. Bacterial toxins (e.g. *Clostridium*) are occasionally suggested, although not proven, as a cause. The fluid loss in these patients can be dramatic, with high replacement rates required in the initial phase. These patients lose the plasma component of blood directly into the intestinal lumen and often present markedly hypovolaemic, requiring immediate fluid resuscitation. Rehydration and supportive care result in a prompt resolution of clinical signs in almost all cases. Metronidazole (10–15 mg/kg i.v. q12h) is commonly added to the treatment regimen to treat clostridial organisms, although the effectiveness of this treatment is largely unknown. Other supportive treatments can include antiemetics and gastroprotectants, although many dogs will recover with fluid therapy alone.

Parvovirus

Parvovirus is a common infectious cause of acute vomiting and diarrhoea in unvaccinated puppies and young adult dogs. Staffordshire terriers and Rottweilers may be over-represented. Clinical signs include anorexia, bloody vomiting and diarrhoea, and occasionally collapse in severe cases. Clinicopathological abnormalities typically include neutropenia and hypoalbuminaemia. Diagnosis may be confirmed using faecal point-of-care antigen testing (SNAP test) or polymerase chain reaction (PCR) but patients may be treated empirically if they are unvaccinated and/or have been exposed to ill dogs. While the commercially available SNAP tests are considered highly sensitive and specific (manufacturers' published data

suggest 100/98%), false-negative results can occur. This is often due to the stage of infection. Virus shedding in the faeces does not occur until 4 days post infection and is often absent by day 14, so testing very early in the course of disease has potential to give a false-negative result. Other scenarios inducing a false-negative result can be incorrect storage of the test reagents or mixing of the sample with the conjugate for too long a time. The authors' recommendation is that if parvovirus is highly suspected but the animal tests negative, proper barrier nursing precautions are still taken and the animal tested again at a later date.

Treatment for parvovirus includes intravenous fluids to correct hypovolaemia and dehydration, replace ongoing losses and provide daily maintenance needs. In addition, since these dogs are typically neutropenic and prone to secondary infection, broad-spectrum intravenous antibiotics are recommended, such as clavulanate-potentiated amoxicillin or ampicillin/sulbactam. In puppies with severe neutropenia that develop signs consistent with sepsis, the addition of an aminoglycoside such as amikacin is advisable, provided that the patients' renal values are normal and that adequate hydration can be maintained.

Puppies sometimes develop severe gastrointestinal bleeding and ulceration, hence the use of gastroprotectants such as H2 antagonists or proton pump inhibitors is recommended. Sometimes this bleeding, combined with loss from blood sampling, can be severe enough to warrant transfusion with whole blood or packed red blood cells (see Chapter 14). Oncotic support is sometimes required due to massive protein loss; this can be provided either with an artificial colloid such as a hydroxyethyl starch product, or with plasma transfusion. Note that large volumes (40–60 ml/kg) of plasma are required to increase albumin levels significantly. There is a significant risk of volume overload or transfusion reaction with this strategy, and patients must be closely monitored.

Antiemetic drugs are usually required to control vomiting and allow enteral feeding. Nutritional support is important, and should be initiated as soon as the dog is able to tolerate even a small amount of enteral feeding. Often a nasogastric or naso-oesophageal tube (Figure 11.6) is required in the early stages. Total or partial parenteral nutrition is an option for severely affected puppies that are unable to tolerate oral feeding; however, a small amount of enteral feeding is essential for enterocyte nutrition and intestinal healing.



11.6 Correct placement of a naso-oesophageal tube in a dog for provision of enteral nutrition. Note that orthogonal radiographs should be obtained to ensure correct placement of the distal end of the tube within the oesophagus.

Other therapies occasionally employed in the treatment of canine parvovirus include recombinant feline interferon-omega. This drug, while not widely used, has shown efficacy in experimental situations (Ishiwata *et al*., 1998; Martin *et al*., 2002; de Mari *et al*., 2003). It has not been fully evaluated in clinical trials and is expensive so is not routinely used in clinical cases.

Potential complications of parvovirus may include aspiration pneumonia or development of intussception. Dogs are ideally treated as in-patients, although in cases with financial constraints, outpatient therapy may be lifesaving. Although these patients may be very unwell, prognosis with appropriate intensive care and fluid management is good.

Pancreatitis

Pancreatitis is caused by severe inflammation of the pancreas leading to autodigestion of the organ by pancreatic enzymes. Clinical signs are typically vomiting accompanied by abdominal pain, although diarrhoea can also occur. A typical history includes a change to a diet high in fat, or consumption of an unusually high-fat meal in the day or two prior to presentation, although some patients will not have a specific change in dietary history. Physical examination findings can include abdominal pain, especially that localizing to the cranial abdomen, and dehydration or hypovolaemia due to intractable vomiting and systemic inflammation.

Laboratory analysis often reveals dehydration indicated by high PCV and total protein. Increases in liver enzyme activity (aspartate aminotransferase (AST)/alanine aminotransferase (ALT)) may be seen. In severe cases, obstruction of the bile duct as it enters the duodenum will give a cholestatic appearance to biochemical analysis, with marked increases in alkaline phosphatase (ALP), cholesterol and bilirubin. Typically, a pre-renal azotaemia can be seen, although acute kidney injury can also occur. Amylase and lipase are not reliable indicators of pancreatitis; pancreatic lipase immunogenicity is more specific. The cPLI test is available as both a reference laboratory test and as a SNAP test. For both tests a value of >400 μg/l is considered consistent with pancreatitis and a value of 200–400 μg/l is considered suspicious. A value lower than 200 μg/l is considered normal. The SNAP test and reference laboratory test have reasonable correlation between them, especially for values >400 μg/l; however, borderline results can be difficult to interpret. The SNAP cPL assay has reported sensitivity/specificity of 92–94%/71–78%, making false positives relatively common. It is, however, useful as a 'rule-out' test. Neither cPLI test has been investigated adequately in dogs with other forms of gastrointestinal disease; anecdotally, clinicians have reported false positive results in animals with inflammatory bowel disease or acute gastroenteritis – this may be due to clinically insignificant pancreatic inflammation or concurrent pancreatitis. Complete blood count findings often include neutrophilia or, less commonly, neutropenia. Radiographic findings include a loss of detail in the right cranial quadrant of the abdomen, widening of the angle between the pylorus and the duodenum, and displacement of the stomach to the left (see Chapter 12). In very severe cases, the duodenum can appear corrugated due to its proximity to the pancreas. Abdominal ultrasonography can demonstrate peritoneal effusion, especially localized to the area around the pancreas, hyperechoic peri-pancreatic fat, and a hypoechoic pancreas. If suspicion exists of a pancreatic abscess or septic process, then ultrasound-guided aspirates of pancreatic lesions or peri-pancreatic fluid can be helpful in confirming this.

Some mildly affected patients will recover with 48 hours of basic supportive care, usually fluids, antiemetics and analgesics if indicated. More severe cases can have a protracted clinical course. In these more severe cases, in addition to adequate fluid therapy, antiemetics and analgesics, nutritional support is often required. If the patient will tolerate enteral feeding with a low-fat diet then this is ideal; if not, then placement of a central catheter and administration of total parenteral nutrition is recommended if the patient is unable to eat after 3–5 days.

Serial examination of vital signs and repeated laboratory testing is required to monitor the progress of these patients. Development of icterus can be a serious complication and warrants ultrasonographic assessment for bile duct obstruction. In this scenario, percutaneous drainage of the gall bladder under ultrasound guidance or surgical stenting of the bile duct may be required. Although most patients will recover from pancreatitis, serious cases can be associated with development of systemic inflammatory response syndrome and multi-organ failure, which carries a very guarded prognosis.

Pancreatitis in cats is a much more challenging disease to identify than that in dogs. Cats are commonly affected with a syndrome called triaditis, which refers to the syndrome of inflammatory bowel disease, inflammatory liver disease and pancreatitis (Simpson, 2015). Most cats with triaditis/pancreatitis have a chronic history of anorexia, vomiting and diarrhoea, and less commonly present with acute abdominal signs.

Diagnosis of pancreatitis in cats may be challenging; routine testing of amylase and lipase is of no value in confirming a diagnosis. A point-of-care test for feline pancreatic-specific lipase (SNAP fPL test) is available and can be utilized to improve the likelihood of diagnosis. Ultrasonography is very useful for identification of pancreatic disease in cats, as well as assessing the liver and intestinal tract.

Treatment of pancreatitis in cats includes supportive care and early nutritional support. As most cats have concurrent inflammatory disease affecting the liver and gastrointestinal tract, hyporexia is commonly long-standing. Nutritional support may include TPN, PPN, or preferably enteral nutrition with either a naso-oesophageal or oesophageal tube. Cats commonly develop chronic pancreatitis and owners should be advised of this risk.

Gastrointestinal ulceration

Gastric or duodenal ulceration typically presents as a patient having haematemesis or melaena. Other differentials for this presentation include parasitism, parvovirus, coagulopathy (especially thrombocytopenia), Addison's disease or gastrointestinal neoplasia. Gastrointestinal ulceration can be commonly associated with excessive or prolonged treatment with non-steroidal anti-inflammatory drugs (NSAIDs), especially if these are used concurrently with steroids. Local gastrointestinal tract disease, such as severe inflammatory bowel disease or gastrointestinal neoplasms, can also be precipitating factors. Ulceration can also occur secondary to excessive histamine release, for example, from cutaneous mast cell tumours. Animals with other critical illnesses such as sepsis are also at high risk of developing ulcers.

Physical examination findings often include abdominal pain and melaena on rectal examination. Radiographic findings include the presence of a fluid-filled stomach and intestines. If an ulcer is perforated and is causing a secondary septic peritonitis (see Chapter 12) then a loss of abdominal detail may be appreciated, which can be confirmed via ultrasonography or abdominocentesis. Ultrasonography findings can be non-specific; it is occasionally possible to visualize changes in wall layering associated with an ulcer, however, this can be challenging. Confirmation of the diagnosis or further work-up should signs not resolve could include barium contrast radiography or upper gastrointestinal endoscopy to visualize a bleeding ulcer or to rule out other causes such as a mass.

Treatment is mainly supportive. Gastroprotectants such as proton pump inhibitors are recommended for patients with bleeding ulcers. If the patient is not vomiting or the vomiting can be controlled with antiemetics, then sucralfate is also often prescribed. Pain should be managed with opioid analgesics as NSAIDs should be avoided in these patients. Recent evidence has shown proton pump inhibitors, when given twice daily, to be superior to other gastroprotectants at maintaining a gastric pH in a range that is conducive to ulcer healing. Other gastroprotectant medications that have been evaluated include H2 blockers, especially famotidine and ranitidine. While these are in widespread use, their value in gastric ulcer treatment may be limited. Some clinicians will use misoprostol in cases of gastric ulceration – while there is no clinical evidence of its efficacy, it may be reasonable to use in cases where prostaglandin synthesis is impaired, such as in NSAID-induced gastric ulceration.

Fluid therapy should be provided to maintain adequate hydration. Blood transfusions may be required to manage symptomatic anaemia (see Chapter 14). In the rare case of catastrophic haemorrhage, then haemostatic resuscitation techniques can be employed (see Chapter 12) involving the use of packed red blood cells and plasma or whole blood to avoid development of, or to treat, a coagulopathy. If there is a focal site of haemorrhage and no response to supportive care, surgical intervention to resect the bleeding ulcer has also been reported with some success. Bleeding masses usually require surgical resection.

Regurgitation

Regurgitation indicates the presence of oesophageal (usually intrathoracic) disease. Although idiopathic megaoesophagus occurs occasionally, regurgitation is often secondary to another disease process. Severe regurgitation can occur in young animals with anatomical defects such as vascular ring anomalies; other causes include oesophageal stricture, oesophageal foreign body (see Chapter 12), severe oesophagitis or, rarely, hypoadrenocorticism or myasthenia gravis. Sometimes animals with gastric disease can also present with regurgitation as the primary complaint, often because of reflux oesophagitis, but active vomiting is much more common in animals with gastric disease. Any disease resulting in ileus can ultimately cause regurgitation.

Management of regurgitation involves identifying the underlying disease. Standard laboratory testing and radiographs (including thoracic radiographs to assess the oesophagus) are usually adequate. Management is by reducing acid reflex using proton pump inhibitors or H2 blockers, use of sucralfate slurries to treat oesophageal ulceration, and improving motility with medications such as metoclopramide or erythromycin, as well as treatment of the underlying disease. Use of metoclopramide is controversial because it tightens the lower oesophageal sphincter, and therefore can worsen regurgitation in some patients; it is often best to use this drug on a trial basis, assessing individual response before deciding whether to

continue therapy. Patients with vascular ring anomalies require surgical management that is outside the scope of this chapter. Complications of regurgitation include oesophagitis, oesophageal stricture and aspiration pneumonia.

Parasitic enteritis

Parasitic enteritis is very common in young puppies and kittens but can also occur in adults. Common culprits include roundworms, whipworms, *Giardia* and coccidia. Patients can present with vomiting or persistent diarrhoea, which may be bloody. Whipworms can cause significant blood loss and resultant melaena. Laboratory testing may be unremarkable or may show anaemia (which can be microcytic/hypochromic if it is a chronic problem) and low total protein due to intestinal blood loss. Other differentials for young animals include non-specific gastroenteritis or parvovirus. Definitive diagnosis is by faecal flotation and smear, with identification of the parasite ova or oocysts. Treatment with fenbendazole at 50 mg/kg orally q24h for 3 days is effective against most roundworms and whipworms, as well as *Giardia*. Management of coccidia usually requires treatment with sulfadimethoxine at 50 mg/kg orally on the first day followed by 25 mg/kg orally q24h for 14–21 days. Other supportive care such as fluid therapy, gastroprotectants and blood transfusion may be required as well as owner education to prevent further incidences.

Hypoadrenocorticism (Addison's disease)

Patients with Addison's disease can present with acute or chronic gastrointestinal signs, or simply lethargy and inappetence. They can be mildly to severely affected. Patients in a severe Addisonian crisis will present with signs of cardiovascular shock and in most cases with the typical electrolyte abnormalities of hyperkalaemia (which can be high enough to be life-threatening) and hyponatraemia. Hypoglycaemia, which can be severe enough to cause clinical signs, also occurs.

In these patients the priority is managing hypovolaemic shock and treating for hyperkalaemia (see Chapter 5). Treatment is usually with intravenous boluses of isotonic crystalloids, along with specific treatment for hyperkalaemia, including administration of calcium gluconate (50–100 mg/kg slowly i.v.), insulin with dextrose or dextrose alone. Acid–base abnormalities should be corrected with aggressive fluid therapy and occasionally bicarbonate. In many cases fluid therapy alone is sufficient to lower the potassium. Other newer treatments for hyperkalaemia may include beta-agonists such as terbutaline. Confirmation of hypoadrenocorticism is by ACTH stimulation testing. Following initial stabilization, treatment with a supraphysiological dose of dexamethasone (0.15–0.25 mg/kg i.v.) is recommended. Other steroids can be used, such as hydrocortisone or prednisone. While these steroids are extremely effective, they will interfere with the cortisol assay so their use should be delayed until the ACTH stimulation test has been performed (see Chapter 16).

Acute colitis

Sudden onset large bowel diarrhoea is a common reason for dogs and cats to present to the emergency room. Colitis is characterized by straining to defecate and production of small amounts of soft or liquid faeces, which often contain mucous. Sometimes this can progress to blood being present in the faeces, which is often the reason for owners presenting their pets for veterinary care. A thorough physical examination including rectal examination should be performed – in most cases the examination is normal save for the finding of diarrhoea. Extensive work-up is rarely required; mild to moderate colitis usually will not cause an animal to be systemically unwell, although if it is severe or certain infective agents such as *Salmonella* are involved then the patient could be considerably more compromised. A detailed history is important to assess parvovirus vaccination status, exposure to other dogs and any history of dietary indiscretion.

Most cases of colitis alone are caused by dietary indiscretion or stress and will be self-resolving. Parasitism is not uncommon, especially *Giardia*, so faecal flotation or specific *Giardia* testing may be indicated in some cases, especially if the dog has recently been kennelled. If the dog is systemically unwell then more extensive work-up such as bloodwork to assess white count and faecal cultures in case of *Salmonella* infection can be useful tests to direct therapy. There is some (albeit controversial) evidence that clostridial overgrowth can cause acute colitis, so some clinicians choose to treat these patients with metronidazole, especially if bloody diarrhoea is present. While this is a common practice, there is little evidence of its efficacy. Antibiotic-responsive colitis has been described in Boxer dogs (histiocytic ulcerative colitis); however, this tends to be a more chronic condition that the dog's owners will likely be aware of.

In cats, *Tritrichomonas* is a protozoan parasite associated with development of severe colitis, often accompanied by weight loss and systemic illness if left untreated. This is most commonly seen in multi-cat households or shelter situations and can be diagnosed by faecal PCR or examination of very fresh faecal samples. In general, treatment of acute colitis consists of ensuring adequate parasite prophylaxis and supportive care. For sicker patients or those with bacterial pathogens, further work-up including bloodwork and faecal PCR may be needed to reach a diagnosis. Antimicrobial use should be reserved for patients with a known or highly suspected bacterial aetiology for their disease.

Hepatobiliary disease

This covers a wide range of disease affecting the liver, gall bladder and bile ducts. Diagnostic testing focuses on first differentiating obstructive from non-obstructive disease. Generally, obstructive biliary disease requires interventional (typically surgical) management whereas non-obstructive disease can be managed medically. Animals with peracute-onset hepatobiliary disease will commonly present for vomiting, inappetence or abdominal pain. Physical examination will often confirm cranial abdominal pain, although it is not always present; dehydration and jaundice may also be present depending on the degree of illness and chronicity. Sudden acute collapse can be seen in patients with very severe disease such as portal vein thrombosis, or due to seizures secondary to hepatic encephalopathy. If ascites is present, a fluid wave may be palpable. Occasionally, melaena secondary to gastrointestinal ulceration can be found.

Typically, diagnostic testing starts with bloodwork. Complete blood count can be helpful, especially to look at white cell counts and morphology if there is concern for acute hepatitis. Platelet count and coagulation times are also important to assess as many patients with acute liver disease, especially if it has progressed to liver failure, are coagulopathic. This is important information to have, especially if sampling of the liver is to be performed. The

chemistry profile is most helpful in determining severity and type of liver disease. Bilirubin levels alone can be misleading as increases in bilirubin could come from pre-hepatic haemolysis (such as immune-mediated haemolytic anaemia), hepatic (such as neoplasia) and post-hepatic (bile duct obstruction of any cause) causes, so do not always indicate primary liver disease. The clinician may appreciate a cholestatic pattern – high bilirubin, high ALP, high gamma-glutamyl transferase (GGT) and high cholesterol in cases of bile duct obstruction or severe gall bladder disease such as a mucocoele. In cats, ALP has a very short half-life and so an increase is always significant. Dogs can have increases in ALP for a number of non-hepatic reasons, including steroid use and hyperadrenocorticism. Alternatively, a pattern more consistent with hepatic parenchymal damage may be seen, consisting of increases in ALT and AST activity indicating direct cellular damage. Unfortunately, the degree of rise in liver enzyme activity does not always correlate with the severity of the liver injury. To assess for very severe liver damage causing liver failure, it is important to look at markers of liver function. On the chemistry profile these include glucose, blood urea nitrogen and albumin. Decreases in these, especially if combined with coagulopathy, indicate liver failure and a guarded to poor prognosis dependent on the underlying cause. For coagulation testing, ACT, PT or PTT can be used. PT is the most sensitive for liver failure-induced coagulopathy as typically factor VII is depleted first. Thromboelastography changes have also been described in liver disease and can be especially helpful in assessing for hypercoagulability; however, these tests are still not widely available outside referral centres. Ammonia is a helpful test in assessing liver function – an elevated ammonia level is commonly found in animals with significantly reduced liver function such as that seen with portosystemic shunt or acute liver failure. Serial ammonia assays can be used to track the success of therapy for hepatic encephalopathy. Bile acids are of limited value in the assessment of acute liver disease as many of the animals presented for care will have elevated bilirubin – if, however, the bilirubin is not high then bile acids are a useful test for assessing for adequate liver function.

Imaging can be helpful in assessing the size and shape of the liver. For this purpose abdominal radiographs are excellent. Radiographs may also show choleliths, liver masses or more unusual lesions such as free gas in the liver indicating abscessation. Ultrasonography allows a more detailed assessment of the liver parenchyma, with the ability to assess for homogeneity, nodules and masses as well as the vascular system, especially the portal vein. It is critical for diagnosis of biliary obstruction and gall bladder disease (see Chapter 12). Ultrasonography also allows for guided sampling of lesions for cytology and culture, which can be extremely helpful in the work-up of the patient's disease.

Acute hepatic necrosis

Acute hepatic necrosis caused by toxins is a relatively common presentation of liver disease in the emergency setting. In this syndrome, an ingested toxin – often medication such as NSAIDs or other toxins such as xylitol or sago palm, cause direct damage to the hepatocytes – with extensive necrosis. Clinical signs are usually extreme lethargy, inappetence and vomiting, sometimes with associated abdominal pain. If enough of the hepatocytes are damaged then acute liver failure (ALF) will result. If ALF occurs, other clinical signs such as melaena due to coagulopathy, oedema and ascites due to hypoalbuminaemia, and altered mentation due to hepatic encephalopathy will occur. The treatment for these patients is to first remove any existing toxin through gastrointestinal decontamination (see Chapter 19). Unfortunately, many hepatotoxic compounds have extensive first pass metabolism and will be removed entirely by the liver; they are then excreted in bile, where they can be re-absorbed from the intestine. To prevent this, using multiple-dose activated charcoal every 6–8 hours or binding compounds such as cholestyramine has been recommended. Subsequent treatment is mainly supportive, providing adequate fluid replacement, maintaining electrolyte balance and supplementing glucose and clotting factors by plasma transfusion where required. Secondary complications include gastrointestinal ulceration, and many clinicians will treat with a proton pump inhibitor for ulcer prophylaxis. Vitamin K therapy is helpful if the animal is coagulopathic but recent evidence of hypercoagulability in many animals with liver disease means that this should ideally be guided by coagulation testing. In the event that the animal is encephalopathic, specific treatment for this must be instituted. Antibiotics, typically penicillin, if given by injection can reduce the bacterial load in the intestine, which is the source of much of the absorbed ammonia. Lactulose can also be administered either orally or as an enema – lactulose traps ammonia within the intestinal lumen, preventing its absorption. In very severe cases of hepatic encephalopathy causing cerebral oedema, mannitol may be administered but only after adequate fluid resuscitation. If the animal recovers, regular rechecks with bloodwork are often needed and potentially hepatotoxic drugs should be avoided in the future.

Bacterial hepatitis/cholangiohepatitis

Bacterial hepatitis or cholangiohepatitis is common, especially in cats. It is typically caused by ascending infection from the bile duct into the gall bladder. *Escherichia coli* and anaerobic bacteria are commonly identified bacterial agents and antimicrobial therapy should be tailored accordingly. These animals will present with significantly increased AST/ALT with bilirubin, ALP and GGT increases depending on the degree of involvement of the biliary system. They may have a high or low white blood cell count and will sometimes have fever. Severe cases can present with severe sepsis or septic shock, although most will not be this severe at the time of initial presentation. Clinical signs, laboratory testing and response to therapy can all be used to achieve a diagnosis of bacterial hepatitis/cholangiohepatitis. Positive cultures (blood, liver aspirates or gall bladder aspirates) are definitive, although the majority of cases are managed successfully without these tests. Culture is always indicated in animals that have relapsed, have recently been exposed to antimicrobials for another reason, or where response to therapy is lacking. Ultrasonography may show a slightly enlarged, hypoechoic, swollen liver, or imaging could be normal. Findings of gallstones which could be acting as a nidus of infection is supportive of the diagnosis. Treatment involves good supportive care, fluid therapy, liver protectant medications such as *N*-acetylcysteine and broad-spectrum antibiotic cover. A potentiated penicillin such as ampicillin/sulbactam may be sufficient in mild to moderate cases as it provides broad-spectrum cover including against anaerobes. In severe cases, combination therapy with a penicillin such as ampicillin or a potentiated penicillin with a fluoroquinolone and metronidazole could be considered. Note

that while fluoroquinolones have excellent penetration to the biliary system, their addition to an antibiotic protocol has not been clinically established to be more effective than appropriate monotherapy. If animals respond to treatment and bacterial hepatitis is confirmed or highly suspected then antibiotic treatment should be continued for at least 6 weeks.

Leptospirosis

Leptospirosis can cause an acute hepatitis, sometimes alone but often with involvement of other organs such as the kidneys. Leptospirosis itself can cause coagulopathy, so it is difficult to distinguish the direct coagulopathic effect of the organism from the concurrent liver damage. In general, liver damage caused by leptospirosis is reversible given appropriate treatment and prognosis is fair to good even in very sick animals. Treatment is typically good supportive care including provision of nutrition and appropriate antibiotics – most clinicians will use penicillin followed by a 3-week course of doxycycline. Strict barrier nursing should be in place during the initial treatment due to the zoonotic potential. Diagnosis can be by PCR on blood or urine samples or by measurement of antibody titres.

Hepatic neoplasia

Certain neoplasias such as lymphoma may infiltrate the hepatic parenchyma and have similar clinical appearance and biochemical changes to an acute hepatitis. Lymphoma especially can be rapidly progressive. Typical biochemical changes are often accompanied by a non-regenerative anaemia, which can be mild or severe. Definitive diagnosis is by aspirate or biopsy of the liver. Treatment is with standard chemotherapy agents; however, in animals with extensive hepatic involvement, remission occurs less frequently and tends to be shorter, making the prognosis guarded to poor.

Other tumours such as haemangiosarcoma or hepatocellular carcinoma may affect the liver. These can cause vomiting due to compression of surrounding structures or can bleed acutely, causing an acute abdomen and cardiovascular collapse. See Chapter 12 for surgical management of abdominal tumours.

Biliary obstruction

Conditions causing bile duct obstruction such as gall bladder mucocoele, severe pancreatitis or pancreatic or duodenal masses can lead to patients presenting with signs of acute abdominal disease (inappetence, vomiting, abdominal pain, collapse) along with icterus. Typically, on bloodwork, hyperbilirubinaemia is seen with the liver enzymes demonstrating a cholestatic pattern. Diagnosis is usually by abdominal ultrasonography. Percutaneous or surgical intervention is usually required in severe cases (see Chapter 12).

Portal vasculature

Conditions affecting the portal vasculature can present as an emergency. Animals with acute portal vein thrombosis are often extremely unwell, with severe bloody diarrhoea and vomiting, abdominal pain, cardiovascular collapse and sometimes ascites. These patients should be stabilized with aggressive fluid therapy while the diagnosis is confirmed, typically by abdominal ultrasonography. Treatment is by cardiovascular support and treatment of the thrombus. Typically, thrombolysis with tissue plasminogen activator is recommended, although some clinicians opt for surgical thrombectomy. Prognosis is guarded to poor in severe cases. Severe portal hypertension can also be seen after attenuation of a portosystemic shunt (PSS); similar signs of vomiting, diarrhoea, cardiovascular collapse and abdominal distension can be seen. Treatment is with cardiovascular support and emergency reversal of the attenuation surgery.

Occasionally, vomiting and diarrhoea can be the major presenting complaint for animals with PSS or microvascular dysplasia (MVD); however, neurological signs are typically also present either at the time of examination or historically. These conditions can be diagnosed in young or older animals. Typically, these animals are 'poor doers', may exhibit neurological signs, especially after eating, seem sleepy or have frequent gastrointestinal upset. Abnormal bile acids may also raise suspicion for a PSS or MVD in an animal with compatible clinical signs. Definitive diagnosis of PSS requires visualization of the shunt with ultrasonography, contrast CT or at surgical exploration. Diagnosis of MVD requires exclusion of PSS and liver biopsy. Treatment consists of managing hepatic encephalopathy, supportive care for gastrointestinal signs and nutritional management (e.g. low-protein diet). Occasionally, animals with hepatic encephalopathy develop seizures; these should be managed with anti-epileptic medications – typically either levetiracetam or potassium bromide is used to avoid the hepatotoxic side effects of phenobarbital. Note that potassium bromide should not be used to treat cats due to the risk of development of asthma. PSS should be surgically corrected once the animal is stable.

A wide range of other diseases affect the liver; however, they tend to be more chronic – cirrhosis, copper-associated hepatopathy and immune-mediated hepatitis all occur in small animals but are outside the scope of this chapter.

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Chapter 12

Acute abdominal and gastrointestinal surgical emergencies

David Holt and Gareth Buckley

Abdominal and gastrointestinal surgical emergencies include a diverse group of conditions that can be challenging to diagnose and manage successfully. Initially, the animal must be carefully evaluated and appropriate resuscitative measures commenced. Once a diagnosis is made, resuscitation is continued to stabilize the animal prior to anaesthesia. Emergency surgery requires a complete exploratory laparotomy, critical evaluation of tissue viability, and exacting surgical technique for best results. Adept postoperative management, including careful monitoring and an index of suspicion for potential complications, is vital.

Initial examination and resuscitation

Dogs and cats frequently present for emergency evaluation because of acute vomiting or regurgitation, with or without diarrhoea. Each animal must be carefully evaluated to determine if it has a true emergency problem requiring extensive resuscitation, diagnostic investigation and possibly emergency surgery. A rapid initial examination should be performed at presentation to evaluate the animal's degree of dehydration and hypovolaemia, and to exclude imminently life-threatening conditions including severe aspiration pneumonia, shock and sepsis. An initial emergency database, performed on blood withdrawn during catheter placement, includes measurement of packed cell volume (PCV), total solids (TS), renal values, blood glucose, serum electrolytes, acid–base and ideally serum lactate levels. Initial resuscitation is started based on this information, and then a thorough history is compiled and a complete physical examination is performed.

History

History obtained from the owner should include questions about the animal's vaccinations, worming history, previous medical conditions, the possibility of foreign body ingestion, the recent ingestion of rubbish, refuse, or a fatty meal, and possible exposure to toxins (e.g. heavy metals including lead, ethylene glycol) or medications (corticosteroids, non-steroidal anti-inflammatory drugs (NSAIDs), paracetamol). It is important for the veterinary surgeon (veterinarian) to try to distinguish between vomiting and regurgitation from the history. Vomiting is characterized as an active retching process with repeated contractions of the abdominal muscles. Regurgitation is often more passive, with owners reporting that the animal 'opens its mouth and the food falls out'; this tends to indicate oesophageal rather than gastric or small intestinal disease. Finally, the veterinary surgeon should perform a systems review, questioning the owner about other clinical signs that might indicate an underlying disease process. For example, polydipsia and polyuria might indicate renal disease, pyometra, diabetes mellitus, hypercalcaemia or hepatic disease.

Physical examination

Abdominal and gastrointestinal surgical emergencies include a great range of conditions from oesophageal foreign bodies to peritonitis and rectal prolapse. Physical examination findings vary depending on the nature of the presenting emergency. During physical examination, the veterinary surgeon focuses on:

- The degree of hypovolaemia (loss of intravascular volume, indicated to an extent by the animal's mucous membrane colour, heart rate and pulse quality) and dehydration (the loss of interstitial fluid, indicated by changes in skin turgor and capillary refill time)
- The possibility of a linear foreign body trapped under the tongue of the animal
- A thorough auscultation of the heart and lungs to rule out underlying cardiac or pulmonary disease that might impact fluid therapy and anaesthesia, and to evaluate for the possibility of aspiration pneumonia occurring secondary to vomiting or regurgitation
- Abdominal palpation to evaluate for possible generalized abdominal distension with free gas or fluid, hepatic, gastric, intestinal or splenic distension or malposition, urinary bladder distension (indicating possible obstruction) or absence (indicating possible urinary leakage), the presence of a palpable foreign body or intussusception, and the presence of pain (indicating possible pancreatitis or peritonitis). If possible, the animal's forelimbs are held off the ground during palpation to allow the cranial abdominal contents to slide caudal to the last ribs
- Rectal examination to evaluate the rectum, anal sacs, urethra, prostate (male) and vagina, distal uterus and cervix (female), and to obtain a faecal sample for evaluation for parasites and pathogenic bacteria if appropriate

- A thorough palpation of peripheral lymph nodes and evaluation of the skin for the presence of masses that might be histamine-secreting mast cell tumours.

Overall, the aim of the history, physical examination and ultimately further testing is to assess whether or not the animal has a condition requiring surgery, whether the animal has co-existing disease or complications such as shock or sepsis that need to be addressed prior to surgery and, if surgery is required, how urgently it should be performed.

Initial cardiovascular stabilization

Fluid resuscitation and cardiovascular optimization are crucial, especially in patients that may require subsequent general anaesthesia and surgery. Intravascular volume losses can be significant in patients with surgical abdominal disease in which fluid may be lost into the intestinal lumen, or into the peritoneal cavity (third space loss).

Treatment should begin immediately in cardiovascularly unstable patients. In animals with no previous history of heart disease, no respiratory abnormalities, and no murmur or abnormal lung sounds evident on initial examination, up to 90–100 ml/kg (dogs) and 50–60 ml/kg (cats) of balanced electrolyte solution may be administered intravenously in the first 60 minutes. This is typically given in aliquots of 20–30 ml/kg, with reassessment of the patient's cardiovascular and pulmonary parameters after each aliquot (see Chapter 4). Endpoints of resuscitation include normalization of heart rate, pulse quality, blood pressure, mucous membrane colour and mentation. In addition, markers such as lactate and urine output can be used in conjunction with physical examination parameters to assess adequate fluid resuscitation.

Two large-bore peripheral intravenous catheters are inserted, and where possible, prior to fluid therapy, blood and urine are obtained for an initial database. The PCV and TS are usually increased in non-anaemic animals that are dehydrated, but should be interpreted in light of clinical findings. For example, an animal with a 'normal' initial PCV may actually be quite anaemic following rehydration. Animals with acute haemorrhage may have a normal PCV at presentation. In dogs (but not in cats) with an acute haemorrhagic crisis, the PCV at presentation may temporarily be maintained in the normal range by splenic contraction. The TS, however, drops very quickly and is a better early indicator of the severity of blood loss. As intravenous fluids are given, both the PCV and TS may drop to dramatically low values.

Fluid resuscitation in patients with abdominal bleeding is challenging, and requires care to avoid exacerbating haemorrhage – see treatment of haemoperitoneum, below. Blood transfusion is usually required if the PCV rapidly drops below 25%. In these cases, fresh whole blood or packed red blood cells (PRBCs) (10–20 ml/kg) are administered over 4 hours (see Chapter 14). In severely anaemic, hypovolaemic animals this administration rate can be increased if necessary, and blood products can be bolused rapidly to exsanguinating patients in very severe cases. In this instance, if there are no neoplastic cells in the peritoneal blood, autotransfusion is also an option. Colloids (e.g. plasma, albumin, hydroxyethyl starches) can be considered, however, their use is controversial and there is no evidence that their use improves outcome.

Serum electrolytes and acid–base status are frequently altered in animals with surgical abdominal emergencies. These tests provide valuable information and help determine the appropriate fluid for resuscitation. Animals vomiting gastric contents secondary to a pyloric obstruction will lose sodium, potassium and chloride, and have a metabolic alkalosis associated with hypochloraemia. For these animals, 0.9% sodium chloride supplemented with potassium is the ideal replacement fluid. Animals vomiting because of obstructions lower in the small intestine will lose not only sodium, potassium and chloride but also bicarbonate; their acid–base status can be more variable but is often characterized by metabolic acidosis.

Patient evaluation and diagnostic investigation

The nature and urgency of further diagnostic testing is determined by the findings on physical examination. Further evaluation including blood work and imaging is usually required before a decision can be made on whether surgery is required.

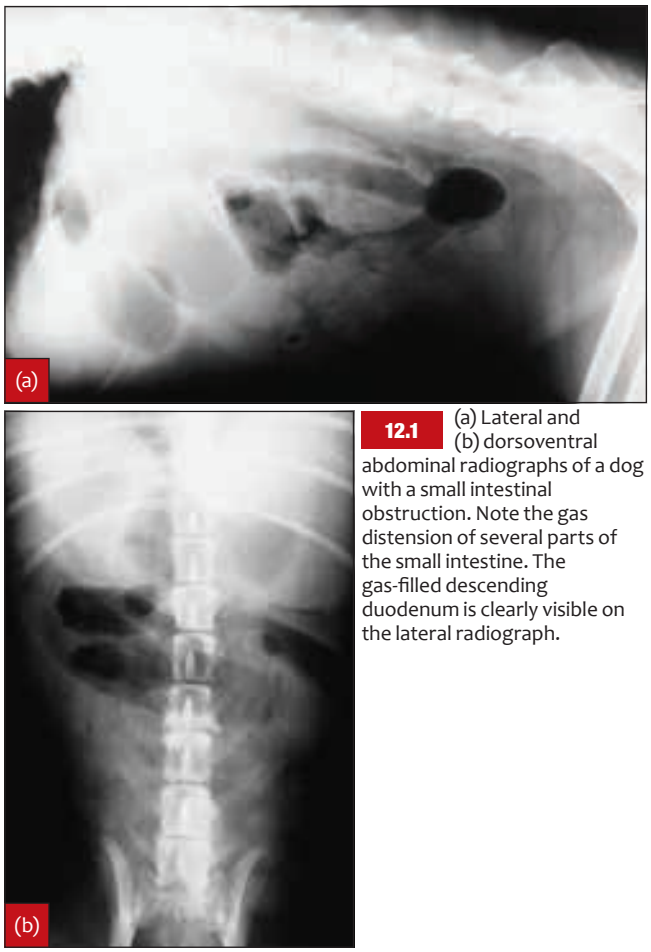
Results from a complete blood count, serum biochemical analysis, and possibly coagulation testing, although not always immediately available, should be part of the diagnostic work-up for any patient being evaluated for possible emergency surgery.

Radiography

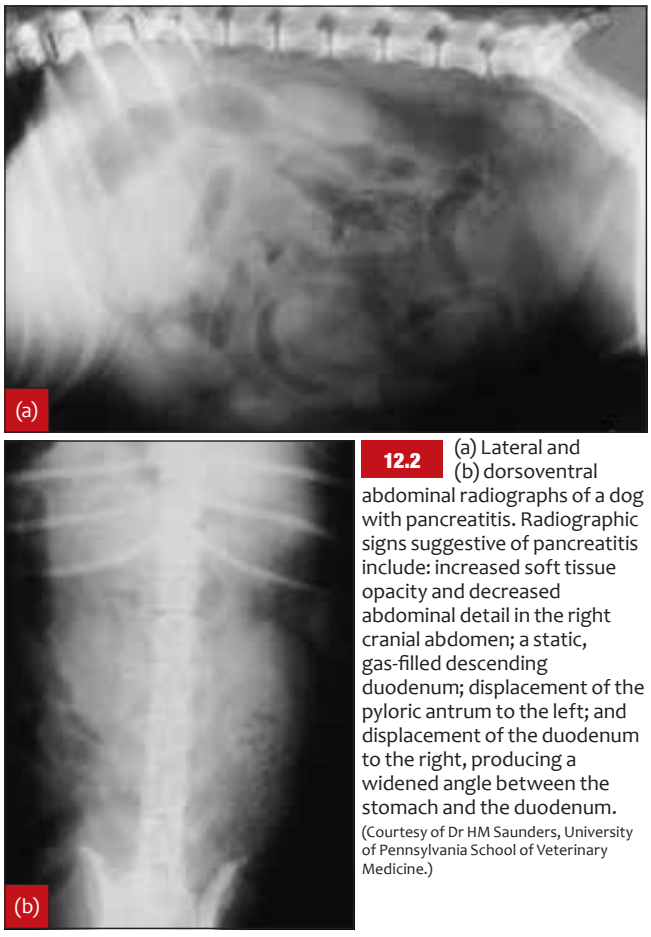
Additional diagnostic tests, such as radiographs, are obtained depending on the results of the physical examination. Plain abdominal radiographs are indicated in animals with abdominal pain or persistent vomiting. Plain cervical and thoracic radiographs should be made to evaluate the oesophagus for foreign bodies in animals presenting with regurgitation. Radiographs should be critically evaluated for evidence of gastrointestinal obstruction, foreign bodies, pancreatitis, masses, and the presence of free air or fluid in the peritoneal cavity. Radiographic signs of obstruction include the presence of gas- or fluid-distended small bowel loops (Figure 12.1; see also Chapter 24). Severe generalized intestinal gas distension can be associated with a mesenteric volvulus. Decreased radiographic contrast in the right cranial abdomen, displacement of the stomach to the left, widening of the angle between the pyloric antrum and the duodenum, displacement of the duodenum to the right and static gas in the duodenum are all radiographic signs associated with pancreatitis (Figure 12.2). Evidence of free gas in the abdominal cavity without prior abdominocentesis or surgery indicates intestinal perforation or the presence of gas-forming organisms in the abdominal cavity, and is an indication for immediate laparotomy. The free gas often accumulates caudal to the diaphragm, outlining the crura of the diaphragm clearly (Figure 12.3). Loss of abdominal detail due to fluid should prompt abdominal paracentesis and peritoneal fluid analysis.

Contrast radiography

Contrast radiographs should be made if gastric or intestinal obstruction is suspected but not definitive on plain abdominal radiographs. Five to 10 ml/kg bodyweight of a 25% liquid barium suspension is given orally. Iodine-based contrast agents (Iohexol, 2–5 ml/kg orally) may be considered if intestinal perforation is suspected, because of concerns that barium may worsen peritonitis if it leaks from the



12.1 (a) Lateral and (b) dorsoventral abdominal radiographs of a dog with a small intestinal obstruction. Note the gas distension of several parts of the small intestine. The gas-filled descending duodenum is clearly visible on the lateral radiograph.



12.2 (a) Lateral and (b) dorsoventral abdominal radiographs of a dog with pancreatitis. Radiographic signs suggestive of pancreatitis include: increased soft tissue opacity and decreased abdominal detail in the right cranial abdomen; a static, gas-filled descending duodenum; displacement of the pyloric antrum to the left; and displacement of the duodenum to the right, producing a widened angle between the stomach and the duodenum. (Courtesy of Dr HM Saunders, University of Pennsylvania School of Veterinary Medicine.)



12.3 Lateral radiograph of a dog with gastric perforation, illustrating free gas in the peritoneal cavity. Note the diaphragm outlined clearly by the lungs cranially and the free peritoneal gas caudally.

gastrointestinal tract. However, radiographs obtained using iodine-based contrast agents may be difficult to interpret because of dilution of the contrast agent. If barium is used and perforation of the intestine has occurred, rapid surgical intervention may prevent any worsening of peritonitis that might occur due to leakage of barium into the peritoneal cavity.

Abdominal paracentesis

Abdominal paracentesis is performed if peritoneal fluid is detected on physical examination or there is loss of detail on plain abdominal radiographs. The ventral abdomen is clipped and prepared as for aseptic surgery. Fluid may be obtained by judicious use of a blind or four-quadrant aspiration technique, or an ultrasound-guided tap can be performed with a 20–22 G needle. Nucleated cell counts should be determined on the retrieved fluid, and it should be examined microscopically for evidence of degenerate neutrophils and the presence of intracellular bacteria. In normal animals, peritoneal fluid nucleated counts before surgery are usually less than 1000 cells/μl. After uncomplicated intra-abdominal surgery, peritoneal fluid neutrophil numbers rarely exceed 10,000 cells/μl. Degenerate neutrophils, with intracellular bacteria, indicate septic peritonitis, and are an indication for immediate exploratory laparotomy. Neoplastic cells in an effusion may be diagnostic.

Peritoneal fluid glucose and lactate levels should be compared with those of the peripheral blood. A peritoneal fluid glucose concentration 1.1 mmol/l lower than that of the peripheral blood or a peritoneal fluid lactate level 2 mmol/l higher than that of peripheral blood is diagnostic for septic peritonitis. These values are not reliable for assessing peritoneal fluid after surgery for peritonitis. Creatinine and bilirubin levels may also be measured on the peritoneal effusion. Values for bilirubin and creatinine that exceed corresponding serum levels indicate biliary leakage or urinary tract leakage, respectively.

Diagnostic peritoneal lavage

In some cases, peritoneal fluid is present but cannot be recovered by paracentesis, because of either lack of reliable ultrasound guidance, loculation of fluid, or plugging of the needle or catheter with omentum. In this situation, diagnostic peritoneal lavage is indicated. The bladder is

expressed and the ventral abdomen is prepared aseptically. An over-the-needle catheter or dialysis catheter is introduced into the abdomen 2 cm caudal to the umbilicus, and 10–20 ml/kg of warm, balanced electrolyte solution is rapidly infused through the catheter. The fluid is distributed by abdominal massage, and then collected. Only a few millilitres of fluid may be retrieved. Contraindications for peritoneal lavage include dyspnoea, diaphragmatic hernia, and severe organomegaly.

Analysis of the fluid should be performed and interpreted in light of the diluting effect of the instilled electrolyte solution. In normal animals, lavaged fluid leucocyte counts before surgery are usually less than 1000 cells/μl. After uncomplicated intra-abdominal surgery, lavaged fluid neutrophil numbers generally increase to 10,000 cells/μl or less. Degenerate neutrophils with intracellular bacteria indicate septic peritonitis, and are an indication for immediate exploratory laparotomy regardless of their number.

Abdominal ultrasonography

Ultrasonography is an extremely sensitive technique for assessing the presence of free peritoneal fluid, and this basic application is easily learned. Free peritoneal fluid can be reliably detected in dogs by use of the aFAST (abdominal focused assessment with sonography for trauma) technique, which was adapted from use in trauma patients. Four sectors of the abdomen are assessed for fluid: the 'cysto-colic' site at the level of the bladder; the 'diaphragmatic-hepatic' site between the liver and diaphragm or between the liver lobes; the 'hepato-renal' site laterally at the right kidney; and the 'spleno-renal' site at the site of the left kidney and spleen. Use of ultrasound guidance can improve the yield of abdominal paracentesis when small volumes of fluid are present (see above).

Abdominal ultrasonography can be used to evaluate the abdominal organs, especially when free peritoneal fluid makes radiographic interpretation difficult. Particular attention should be paid to the pancreas in animals with abdominal pain. The spleen and liver should be carefully evaluated for possible neoplasms or ruptured haematomas in cases of haemoperitoneum, and for evidence of splenic torsion or thrombosis. The biliary tree, urogenital tract (especially the prostate or uterus) and mesenteric lymph nodes should be carefully evaluated.

Ultrasonography can also be helpful for identifying causes of gastrointestinal obstruction which may not be apparent on plain radiographs, such as differentiating between obstruction caused by a foreign body or an intestinal mass. This, however, requires some expertise and experience in ultrasound technique, and if doubt exists then an exploratory laparotomy is recommended to confirm the diagnosis.

Other tests

In animals with respiratory difficulty or possible neoplasia, thoracic radiographs will help confirm suspected aspiration pneumonia secondary to vomiting, or exclude the possibility of metastatic disease. Arterial blood gas analysis will indicate the severity of hypoxia, and a transtracheal or endotracheal wash, if time and patient stability permits, will provide important information on the type and antibiotic sensitivities of bacteria associated with pneumonia. Further evaluation of the vomiting animal could include adrenocorticotropic hormone (ACTH) stimulation tests for hypoadrenocorticism, endoscopy, and/or gastrointestinal biopsies (see Chapter 11).

Exploratory laparotomy

Complete stabilization of the animal with an acute abdominal crisis may not be possible until the underlying cause is treated. In many cases, this requires abdominal surgery. Indications for exploratory abdominal surgery include:

- Free gas visible in the peritoneal cavity of an animal that has not had recent (within 3–4 weeks) abdominal surgery
- Intracellular bacteria and degenerate neutrophils on a peritoneal lavage or tap
- Bilirubin or creatinine levels in the peritoneal fluid greater than those in the serum
- Gastric dilatation–volvulus
- Gastrointestinal foreign body, obstruction (including intussusception or neoplastic in origin), or linear foreign body
- Gastric haemorrhage not responding to medical management
- Animals with abdominal haemorrhage that fail to stabilize or fail to remain stable after initial resuscitation
- Splenic torsion
- Mesenteric volvulus
- Pyometra/prostatic abscessation
- Penetrating abdominal injury (gunshot, impalement).

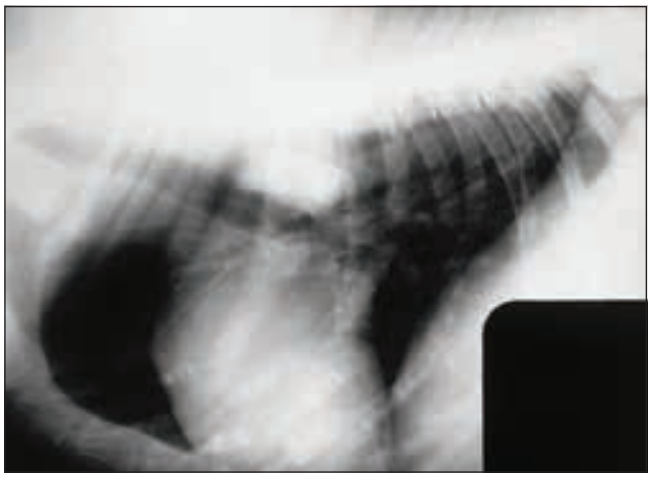
Oesophagus

Oesophageal foreign bodies

Oesophageal foreign bodies should be suspected in any animal presenting with a history of regurgitation or in cases where the owner cannot clearly distinguish between regurgitation and vomiting. Other clinical signs may include gagging, salivation, anorexia and lethargy. Most animals with complete or near-complete obstruction regurgitate food shortly after eating, although they may be able to retain water. Animals may also exhibit signs of pain and/or dyspnoea, coughing and variable depression secondary to aspiration pneumonia. Occasionally, animals may have partial oesophageal obstruction and remain reasonably bright, yet regurgitate after large meals. Oesophageal perforation may occur with sharp foreign bodies. Even relatively blunt bony foreign bodies can cause oesophageal muscle spasm and mucosal necrosis. Necrosis may extend through the entire oesophageal wall causing mediastinitis, pleuritis and pyothorax. It is important to note that the initial radiographic finding with oesophageal perforation is more often a widened mediastinum or pleural effusion rather than pneumomediastinum or pneumothorax.

Foreign bodies tend to lodge at points of oesophageal narrowing, which include the thoracic inlet, heart base and the caudal oesophageal sphincter. In animals with a suspected oesophageal foreign body, the mouth and pharynx should be evaluated and the neck thoroughly palpated. The thorax should be carefully auscultated for crackles or wheezes that indicate aspiration pneumonia. Most foreign bodies are radiopaque and can be visualized on plain cervical and thoracic radiographs (Figure 12.4). Thoracic radiographs are also evaluated for changes compatible with pneumonia. Non-radiopaque foreign bodies require a positive contrast oesophogram using a sterile, water-soluble iodinated contrast agent for visualization.

Foreign body removal should be immediate to minimize the chance of perforation, and is performed using the



12.4 Lateral thoracic radiograph of a dog illustrating a thoracic oesophageal body present over the heart base.
(Courtesy of Dr C Harvey, University of Pennsylvania School of Veterinary Medicine)

simplest means possible. The animal is placed under general anaesthesia and a cuffed endotracheal tube is placed to protect the airway. The area under the tongue is carefully evaluated for a thread or line in animals with a needle or hook lodged in the oesophagus. A flexible fibreoptic endoscope or rigid scope and long, blunt-ended forceps can be used to remove most foreign bodies. Either type of scope must allow insufflation of air to dilate the oesophagus around the foreign body. This must be done with extreme care, and with close monitoring of the animal's blood pressure and ease of ventilation. Insufflation of the oesophagus in an animal with an undiagnosed oesophageal perforation can lead to tension pneumothorax and an immediate life-threatening drop in both oxygenation and blood pressure.

Once the oesophagus has been carefully dilated around the foreign body, the object is grasped with the forceps and rotation is attempted. Often, the foreign body can be carefully withdrawn. However, if it is firmly lodged, excessive traction should not be applied as this may cause or worsen a perforation. An attempt should be made to gently push foreign bodies into the stomach if they cannot be removed. This technique is most applicable to large cartilage foreign bodies that break off small pieces when grasped with forceps, and occasionally extremely large oesophageal hair balls in cats. A large-diameter, well lubricated stomach tube is used to push the foreign body distally. Once in the stomach, bones will generally be digested. Hair balls should be surgically removed.

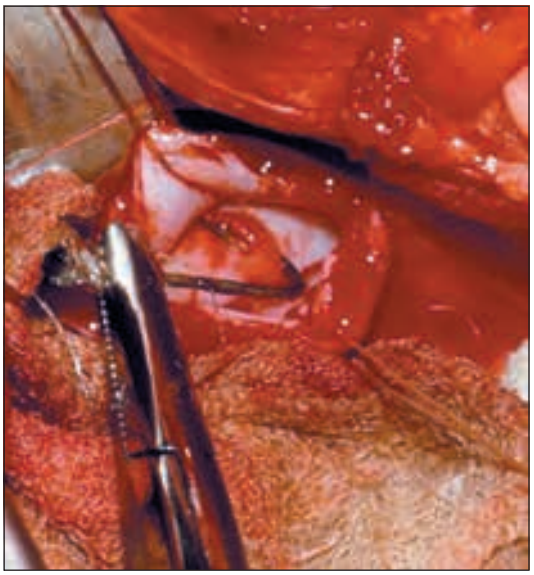
The oesophagus is inspected with the endoscope after foreign body removal. Clean lacerations that do not extend through the full thickness of the oesophageal wall (as judged by gently pushing the tip of a forceps against the laceration through the endoscope) can be left to heal by epithelialization. Full thickness tears or areas of necrotic oesophagus require immediate surgical management.

Surgery is indicated when a foreign body cannot be retrieved or advanced into the stomach, when there is concern that forceps extraction might lacerate the oesophagus and other intrathoracic structures, and when the oesophagus is perforated.

The cervical oesophagus is approached via a ventral midline incision in the neck. The ventral sternohyoideus and sternothyroideus muscles are separated on the midline and the oesophagus is located on the left side of the trachea. For foreign bodies lodged at or cranial to the heart base, a right third or fourth intercostal thoracotomy provides the best exposure of the oesophagus. For foreign bodies lodged caudal to the heart base, a left eighth intercostal thoracotomy approach is used. Although foreign bodies in the distal oesophagus can occasionally be retrieved by manipulation through a gastrotomy incision, this approach is not generally recommended.

Once the oesophagus is visualized, the foreign body is located by palpation. Fish hooks can be difficult to feel in the thoracic oesophagus and occasionally an assistant must locate the hook using an endoscope *per os* while the thorax is open. A longitudinal oesophagotomy is performed (Figure 12.5). The oesophageal wall opposite the incision is checked for perforation, and the incision is closed with a single layer of interrupted, appositional sutures. The authors prefer 1.5–2 metric (4/0–3/0 USP) monofilament suture material. The oesophagus lacks a serosal covering, necessitating careful apposition of the oesophageal layers to prevent dehiscence. Factors that may predispose to oesophageal dehiscence are impairment of its intramural blood supply, tension and motion at the anastomosis site, lack of omentum, general debilitation of the patient, and movement of food and saliva across the oesophageal anastomosis. All tissues must be handled extremely gently. The areas are lavaged thoroughly. Omental, diaphragmatic and pericardial grafts have been used to reinforce the anastomosis. Appropriate enteral nutrition is vital for wound healing and normal immune function. In the nutritionally compromised patient, a gastrostomy tube for feeding is placed via a flank laparotomy.

After uncomplicated endoscopic foreign body removal, food is withheld for at least 12–24 hours followed by introduction of small amounts of soft food or a slurry. Many animals with an oesophageal foreign body will have an uncomplicated recovery; however, a high index of suspicion for complications is necessary as when they occur the consequences can be devastating. For an animal with uncomplicated endoscopic foreign body retrieval, basic treatment for oesophagitis such as gastric acid reduction with H2 blockers or a proton pump inhibitor is indicated. If oesphageal ulceration is present then the addition of sucralfate can be considered. Postoperative regurgitation is relatively common – it is important to differentiate regurgitation due to a minor complication such as oesophagitis



12.5 Longitudinal oesophagotomy performed in the thoracic oesophagus to remove a fish hook. Stay sutures are used to retract the oesophageal wall. The incision is closed with a single layer of single interrupted sutures of 2 metric (3/0 USP) polydioxanone (PDS).

from that associated with more serious complications such as oesophageal stricture. Some animals may develop oesophageal stricture with recurring signs of regurgitation following endoscopic removal of a foreign body, although this is uncommon. Typically, strictures will take several days or weeks to form. The most serious complication of foreign body removal is oesophageal perforation or incisional dehiscence that results in mediastinitis (see below).

Oesophageal perforation

Oesophageal perforation may occur due to chronic foreign body obstruction, ingestion of a sharp foreign body or foreign body removal, direct cervical or thoracic trauma, penetrating bite wounds or oesophagoscopy. Clinical signs of obstruction may or may not be present. Pleuritis, mediastinitis, abscessation, broncho-oesophageal fistulation or cervical cellulitis may occur. Perforation should be suspected in patients with a history of oesophageal obstruction and depression, fever, elevated white blood cell count, cough, dyspnoea or a cervical soft tissue swelling. Diagnosis is by computed tomography, oesophagoscopy or contrast radiography using soluble iodine-based agents. Treatment is initially aimed at stabilizing the potentially septic patient with volume support and intravenous broad-spectrum, bactericidal antibiotics. Leakage of the cervical oesophagus is treated by surgically establishing drainage, controlling the infection and repairing the oesophagus. Thoracic oesophageal perforation requires exploratory thoracotomy, removal of infected debris and repair of the damaged area. The chest cavity is thoroughly lavaged and drained via chest tubes.

In an animal experiencing persistent regurgitation following oesophageal endoscopy or surgery, repeat thoracic radiographs and/or a second-look endoscopy are indicated. Increased respiratory rate or effort, fever or other status change in the patient such as development of anorexia or lethargy should prompt repeat thoracic radiographs to assess for aspiration pneumonia or evidence of pyothorax and mediastinitis (see above). In animals recovering from a thoracotomy for repair of oesophageal perforation, particularly in those with established infection, i.e. pyothorax or mediastinitis, it is vital to pay close attention to cardiovascular parameters, as in any septic patient. These patients will need fluid support, broad-spectrum antimicrobials and pain relief postoperatively. If thoracostomy tubes are in place then daily evaluation of the fluid obtained for cytology and cell count can be valuable for establishing whether dehiscence has occurred. If thoracostomy tubes are not in place then assessment for the presence of mediastinal or pleural fluid by ultrasonography or thoracic radiography is recommended in the event of any adverse change in the patient's status. Nutritional support (see Chapter 22) is important if anorexia persists beyond 1–2 days postoperatively.

Stomach

Gastric dilatation–volvulus

Gastric dilatation–volvulus (GDV) syndrome is a range of conditions that includes gastric dilatation without rotation of the stomach, GDV, and chronic intermittent volvulus with little, if any, dilatation. Although large-breed, deep-chested dogs are 'classically' affected, these conditions can occur in smaller breeds of dogs and have been reported in cats. The exact aetiology of the syndrome is uncertain and probably multifactorial.

Clinical signs in dogs with GDV include non-productive retching, abdominal distension, weakness and collapse. These clinical signs are not specific for the condition and could be associated with other diseases including ruptured splenic haemangiosarcoma or haematoma, splenic torsion, mesenteric volvulus or peritonitis. Physical examination findings vary depending on the severity of the GDV and the associated circulatory collapse, but often include pale mucous membranes, a rapid heart rate, weak, thready pulses and a distended, often tympanic abdomen.

The basis for a rational, effective treatment plan is a thorough understanding of the pathophysiology of GDV. Distension of the stomach with food and swallowed air compresses the portal vein and caudal vena cava. This compression, which leads to decreased venous return to the heart and, in turn, decreased cardiac output, can occur with gastric dilatation only and does not require volvulus. The decrease in cardiac output can be profound, and has been estimated to be 50% of normal in experimental canine models with intra-gastric pressures approximating those seen in spontaneous cases. This decrease in cardiac output leads to decreased tissue perfusion affecting all organs, including the heart. Myocardial ischaemia is one of the main factors cited in the genesis of arrhythmias seen in dogs with GDV. Decreased perfusion to a distended or twisted stomach often leads to gastric necrosis. Gastric decompression and resuscitation can lead to reperfusion injury. Some dogs with GDV are endotoxaemic, presumably because a compromised gastrointestinal mucosal barrier leads to endotoxin absorption into the portal blood and mesenteric lymphatic system.

It is vital to correct the GDV animal's perfusion deficits before anaesthesia and surgery. A rational treatment plan for GDV therefore includes:

- Rapid intravascular volume expansion
- Gastric decompression
- Differentiation of gastric dilatation from GDV
- Surgery once the animal is stable, to reposition the stomach, assess gastric and splenic viability, and attach the pyloric antrum to the right abdominal wall to prevent recurrence of volvulus
- Careful postoperative monitoring for complications, including consumptive coagulopathies and aspiration pneumonia.

Fluids for resuscitation must be administered through cephalic or jugular catheters. Fluid administration through saphenous catheters may be ineffective because the caudal vena cava is obstructed. Two large-bore (16–18 G) catheters are generally placed in the cephalic veins. Balanced electrolyte solutions are administered as boluses for initial resuscitation, typically 20–30 ml/kg followed by assessment of the clinical response. This can be repeated up to a total of 90 ml/kg if required, although it is unusual to require this large a volume of resuscitation fluid (see Chapter 4). Hypertonic saline/dextran solutions can also be used initially (7.5% NaCl, 5 ml/kg i.v., administered over 5–10 minutes), but must be followed by infusion of isotonic crystalloids or colloids to maintain the increase in perfusion. This is an especially effective strategy for rapid resuscitation in very large dogs or where initial vascular access is limited.

Clinical and laboratory parameters, ideally including blood lactate concentrations, are monitored to determine the response to therapy. Blood lactate levels that do not

decrease in response to appropriate resuscitation and decompression indicate a more guarded prognosis.

Once resuscitation is underway, the stomach is decompressed by carefully passing an orogastric tube; in co-operative or very sick animals this can be performed without sedation, in less co-operative animals sedation or preferably a light plane of anaesthesia to facilitate orotracheal intubation is used. The tube must not be forced into the stomach as rupture of the twisted distal oesophagus may occur. If passage of the tube is not possible, the stomach is trocharized. The abdomen is carefully palpated to determine the position of the spleen to avoid laceration during trocharization. A rapid ultrasound scan may be useful if the position of the spleen cannot be determined by palpation. The stomach is trocharized using a large-bore (16–18 G) intravenous catheter. In dogs with extreme gastric distention, relief of some of the pressure by trocharization can facilitate subsequent passage of an orogastric tube. Trocharization should only be performed if the intention is to take the patient to laparotomy.

Radiographs, including a right lateral view, are made to differentiate dilatation from volvulus. In a normal animal in right lateral recumbency, the pylorus lies on the 'down' side of the abdomen, contains no gas and, therefore, is unlikely to be visible radiographically. In many dogs with GDV, the pylorus moves away from the right side of the abdomen and so in right lateral recumbency, the pylorus will be on the 'up' side of the abdomen, contain gas, and, therefore, be visible as a separate gas-filled structure dorsal to the rest of the stomach (Figure 12.6).

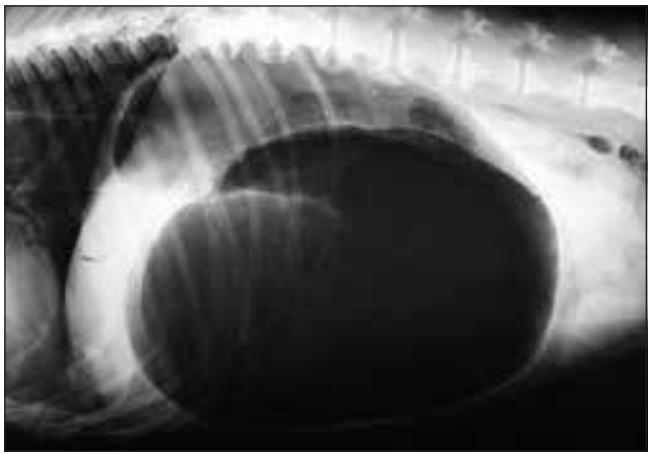
Ideally, anaesthesia is commenced only after the animal has been stabilized (see Chapter 21). At surgery, the stomach is decompressed, derotated and replaced in a normal position. In most dogs, the pylorus rotates from its normal position on the right side of the abdomen, passing between the fundus of the stomach and the ventral body wall to end up either on the left side of the abdomen (180 degree volvulus), dorsal to the rest of the stomach (270 degree volvulus), or towards the right side of the abdomen (360 degree volvulus). The surgeon, standing on the right side of the dog, locates the duodenum and traces it to the pylorus. The pylorus is then gently pulled back into a normal position with one hand, while the other hand gently pushes the remainder of the stomach dorsally to facilitate derotation. The spleen is exteriorized and examined for viability, venous or arterial thrombosis and short gastric vessel rupture. A splenectomy is performed if necessary. The remainder of the abdomen is explored, and then the stomach is re-examined for necrosis, particularly along the greater curvature. As a guide, areas of the stomach that are discoloured dark purple or grey/green, feel paper thin or do not bleed when incised must be removed. If there is doubt concerning the viability of an area it should be removed. Stay sutures are placed in healthy stomach and the necrotic area is resected in stages. The edges of the remaining stomach are examined to ensure they are bleeding and viable. A simple continuous Lembert pattern in the submucosa is initially used to close the stomach. A simple interrupted or continuous Lembert pattern is then used to close the muscularis and serosa. Alternatively, the stomach may be closed with a surgical stapling device (TA-90, 4.8 mm staple cartridge, Covidien-Medtronic) reinforced with a continuous Lembert inverting pattern, oversewing the staple line.

Many procedures have been described to 'pexy' or fix the pyloric antral region of the stomach to the right body wall. The aim is to create a permanent adhesion between the antral region of the stomach and the right body wall to prevent recurrence of volvulus. All of the various techniques work well when performed properly. In straightforward cases, an incisional gastropexy is performed. A 5–8 cm incision is made in the transverse abdominus muscle just caudal to the last rib on the right body wall. A matching, partial-thickness incision is made in the seromuscular layers of the pyloric antrum. The edges of the body wall and pyloric incisions are sutured to each other using polydioxanone (PDS) or polypropylene suture material (Figure 12.7). The abdomen is lavaged with large volumes of a warm, balanced electrolyte solution and closed in a routine manner.

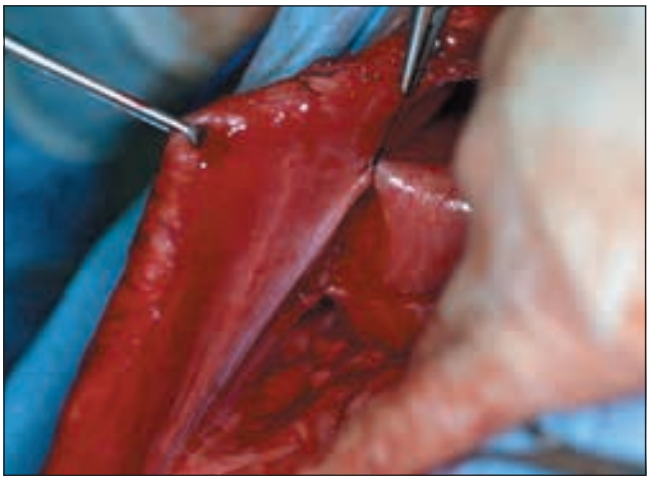
Gastric outflow enhancing procedures have been performed in an attempt to decrease recurrence of gastric dilatation or GDV. Pyloromyotomy and pyloroplasty have been described. However, gastric outflow obstruction is not thought to play a major role in the pathogenesis of GDV. These procedures have not been shown to decrease reccurrence, and have been associated with higher immediate postoperative complication rates and therefore are not indicated.

Gastric foreign bodies

Most gastric foreign bodies are not true emergencies. However, needles should be removed as soon as possible to prevent migration or perforation. Coins which may contain zinc are removed to prevent haemolytic anaemia. In



12.6 Right lateral radiograph of a dog with gastric dilatation–volvulus. Note the appearance of the pylorus in the craniodorsal abdomen as a gas-filled structure.



12.7 Incisional gastropexy with the cranial aspect of the incisions in the body wall and pyloric antrum sewn together.

most cases, this is readily accomplished using a flexible endoscope. Recently, several cases have been reported in which ingestion of a hydrophilic adhesive product ('Gorilla Glue') resulted in severe gastric distension and clinical signs. The product expands on contact with gastric fluids, often encompassing and distending the entire stomach. Removal of this material through a large gastrotomy should be performed as an emergency procedure.

Gastric ulceration

Gastric ulceration and severe haemorrhage is frequently associated with the ingestion of NSAIDs. Other less common causes include gastric neoplasia, mast cell tumours, gastrin-secreting tumours and exogenous corticosteroids. Most of these animals can be stabilized with intravenous fluid therapy, gastroprotectants and transfusions of red blood cells, and the majority do not require surgical intervention. Surgery is considered for those cases with substantial haemorrhage in which medical therapy fails. Rapid endoscopy is useful to differentiate focal bleeding amenable to surgical treatment from diffuse gastric haemorrhage, and to intraoperatively pinpoint the site of the gastric haemorrhage for the surgeon, as this may not be apparent externally. Gastric lavage may be necessary to remove blood clots and allow endoscopic visualization of the gastric mucosa.

Postoperative management following gastric surgery

Patients recovering from complicated gastric surgeries such as GDV correction require extensive treatment and monitoring. Crystalloid and sometimes colloid fluid administration is continued, with fluid administration rates based on clinical (mucous membrane colour, capillary refill time, heart rate, pulse quality, urine output, blood pressure) and laboratory (PCV, TS, serum electrolyte concentrations, lactate concentration) parameters. Colloids (plasma, hydroxyethyl starches, human serum albumin) could be considered in some cases that have hypoalbuminaemia due to dilution, loss into the gastrointestinal system or leakage into the interstitium secondary to systemic inflammation.

Cardiac arrhythmias often become apparent in the first 24–48 hours postoperatively. Postoperative arrhythmias are not necessarily associated with a poorer prognosis, but should prompt the veterinary surgeon to re-evaluate the animal's perfusion status, serum electrolytes and oxygenation. When the arrhythmia is intermittent and not affecting tissue perfusion, no specific antiarrhythmic therapy is required. Antiarrhythmic therapy is started if the arrhythmias are associated with a decrease in tissue perfusion, have a rate greater than 140–160/min, or are associated with severe, potentially life-threatening cardiac electrical conduction disturbances ('R-on-T' phenomenon). An infusion of lidocaine is started (50–70 μg/kg/min) and one or two lidocaine boluses of 1–2 mg/kg are administered to convert the heart to a sinus rhythm (see Chapter 6).

Other complications in the postoperative period include aspiration pneumonia, gastric necrosis, disseminated intravascular coagulation and systemic inflammation/sepsis. Any postoperative GDV dog that becomes febrile, hypovolaemic or depressed should be carefully evaluated for possible gastric necrosis, dehiscence and peritonitis. However, aspiration pneumonia is often overlooked in this situation, as the focus has been on the abdomen during the animal's hospitalization. Many GDV dogs present with histories of retching and vomiting that predispose them to 'silent' episodes of aspiration and subsequent pneumonia. Thoracic radiographs should be made and evaluated for alveolar changes. Treatment of aspiration pneumonia (see Chapter 7) includes oxygen supplementation, nebulization, coupage, and initially broad-spectrum, bactericidal antibiotics administered intravenously. Culture and sensitivity results from an endotracheal or transtracheal wash should direct antibiotic therapy when they are available.

For all patients that have undergone gastric surgery, standard monitoring and support includes adequate nutrition and control of nausea, vomiting or regurgitation, and control of pain associated with surgery. Antimicrobials are generally indicated only in the immediate perioperative period unless the presence of pneumonia, peritonitis or other signs of infection warrant a longer course of treatment.

Small intestine

Intestinal luminal obstruction – foreign bodies and masses

Intraluminal intestinal obstruction is one of the most common indications for laparotomy in dogs and cats, and is most frequently a result of foreign body ingestion. Clinical signs associated with small intestinal obstruction vary with the location, duration and severity of the obstruction. Vomiting, anorexia, depression and abdominal tenderness are common. Vomiting may be frequent and even projectile with a complete proximal obstruction or more sporadic and less profuse with a distal or partial obstruction.

The classic radiographic sign of mechanical obstruction is the presence of multiple loops of gas-dilated small intestine of varying diameters (see Figure 12.1). In animals with complete obstruction, intestinal distension can be severe, particularly if the obstruction is distal. Radiographic changes associated with partial obstruction are less severe and may not be distinguishable from those of gastroenteritis or ileus.

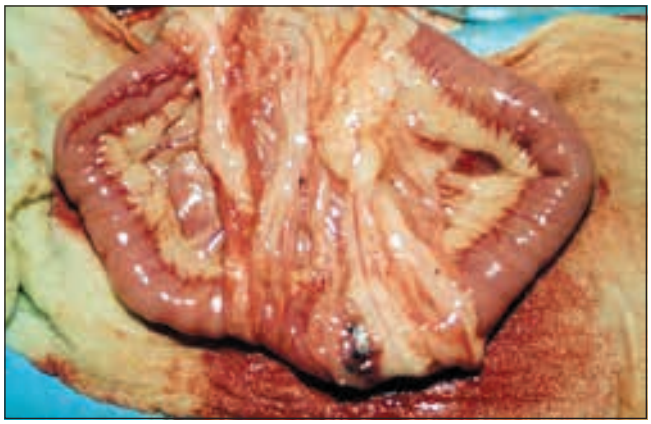
Contrast radiography is occasionally used to provide a definitive diagnosis of intestinal obstruction. Most proximal small intestinal obstructions will be evident within 6 hours after administration of barium suspension; up to 24 hours may be necessary to highlight distal obstructions. Ultrasonography provides a non-invasive and more rapid method of diagnosis, with false positive and false negative rates of 6% and 15%, respectively.

Once a mechanical intestinal obstruction is diagnosed and the animal is stabilized, an exploratory laparotomy is performed and the entire gastrointestinal tract is thoroughly examined. If a foreign body is found and the bowel is relatively healthy, the object is removed through a longitudinal, antimesenteric enterotomy slightly aboral to the obstruction (Figure 12.8). If the bowel wall is necrotic, or if the obstruction is caused by a mass, intestinal resection and anastomosis are performed (Figure 12.9).

The prognosis is usually good after foreign body removal. Resection of non-neoplastic or benign neoplastic masses generally has a better prognosis than resection of malignant neoplasms. The prognosis is usually poor if gross metastatic disease is present at surgery, and life expectancy may be limited to a few months.

Surgical procedure	Suture material	Suture pattern	Technical considerations
Enterotomy	Synthetic absorbable monofilament • 2 metric (3/0 USP) for dogs • 1.5 metric (4/0 USP) for cats	Single layer simple interrupted appositional sutures	
Small intestinal resection and anastomosis		Single layer simple interrupted appositional sutures	Options for managing disparity between luminal diameters of bowel: • Sutures on the larger lumen side can be spaced farther apart than those of the smaller side • The intestine with the smaller lumen can be transected at an angle to create a larger luminal diameter • The intestine with the smaller lumen can be spatulated to create a larger luminal diameter • The lumen diameter of the larger segment can be reduced by oversewing with a simple interrupted Lembert suture pattern
Colonic resection and anastomosis		Single layer simple interrupted appositional sutures	To equalize the lumen sizes in an ileo- or jejunocolonic anastomosis: 1. Oversew the colonic segment in a simple interrupted Lembert suture pattern to slightly invert the colonic mucosa. 2. Incise the antimesenteric border of the jejunum to widen its lumen. 3. Proceed with anastomosis.
Enteroplication	Synthetic absorbable or non-absorbable monofilament • 2 metric (3/0 USP) for dogs • 1.5 metric (2/0 USP) for cats	Simple interrupted sutures placed midway between the mesenteric and antimesenteric borders	• Adjoining segments of intestine are placed side by side in a series of gentle loops to avoid kinking or sharp bends • Complete plication of the jejunum and ileum is recommended because intussusception tends to recur at other sites • Plication of the duodenum is not necessary since intussusception in this area is rare
Colopexy	Synthetic nonabsorbable monofilament • 3 metric (2/0 USP) for dogs • 2 metric (3/0 USP) for cats	Simple interrupted sutures placed between the antimesenteric surface of the descending colon and the left ventrolateral abdominal wall	• Sutures pass through the colonic submucosa

12.8 Recommendations and considerations for surgical procedures used in the treatment of intestinal emergencies.



12.9 Intestinal resection and anastomosis completed. The anastomosis site has been wrapped in omentum.

Intestinal incarceration and strangulation

Intestinal incarceration is an unnatural displacement and entrapment of the intestine. With the exception of intussusception (discussed separately below), it is reported infrequently in the dog. Entrapment usually occurs within inguinal or traumatic body wall hernias. Entrapments in omental tears, congenital hernias, mesenteric rents or subsequent to duodenocolic ligament ruptures have also been reported.

The intestinal lumen may become constricted, resulting in clinical and radiographic signs of mechanical obstruction. If the intestinal blood vessels are also compressed and arterial inflow is inhibited, mucosal degeneration may result in translocation of bacteria and endotoxin into the bloodstream, hernia sac and possibly the peritoneal cavity. Therefore, unlike simple luminal obstruction, incarceration can rapidly progress to strangulation with subsequent intestinal ischaemia and septic or endotoxic shock.

Clinically, animals with strangulation exhibit severe abdominal pain, shock, unexpectedly severe systemic signs, or poor response to stabilization. Treatment of intestinal incarceration includes stabilization of the animal and correction of the intestinal displacement and the initiating cause, with or without intestinal resection (see Figure 12.8). Surgery should not be delayed if strangulation or necrosis is suspected. The prognosis for intestinal incarceration depends on the degree of vascular compromise and the resulting systemic inflammatory response. If extensive areas of the bowel are affected and the systemic inflammatory response has been triggered, the prognosis is guarded to poor. If there is minimal vascular compromise and the animal's cardiovascular parameters are stable, the prognosis is good.

Linear foreign bodies

Linear foreign bodies (e.g. thread, nylon stocking, rope, string, carpet) produce a unique form of intestinal obstruction. The foreign body typically anchors itself around the base of the tongue or at the pylorus. Peristaltic waves carry the remainder of the foreign body aborally, and the intestines progressively gather into accordion-like pleats along the object. As peristalsis continues, the object becomes taut and embedded into the mesenteric side of the intestinal lumen. Untreated, the intestine becomes devitalized, eventually developing multiple, full-thickness perforations of its mesenteric border.

Linear foreign bodies are reported more frequently in cats than dogs. Vomiting, anorexia and depression are the most common clinical signs for both species. Bowel obstruction caused by linear foreign bodies tends to be incomplete, and vomiting may not be as severe or frequent as that seen with complete obstruction. The diagnosis may be delayed because of the non-specific nature of the clinical signs.

The linear foreign body is attached around the base of the tongue in as many as 50% of cats, though it may be difficult to see once it becomes embedded in the lingual frenulum. Linear foreign bodies are rarely discovered under the tongue of dogs during physical examination. On plain abdominal radiographs, the small bowel appears plicated, and is gathered in the cranial to mid-ventral abdomen instead of being dispersed uniformly throughout. Gas collects in small, eccentrically located intraluminal bubbles instead of normal curvilinear columns. After contrast administration, pleating becomes more obvious, and the foreign body may appear radiolucent. After the barium passes into the colon, the foreign body may retain the barium, making it more apparent.

Cats that are clinically stable, have no evidence of peritonitis and present soon after ingestion of lingually anchored foreign bodies have been successfully managed without surgery. After being freed from around the tongue, the string may pass through the gastrointestinal tract in several days. However, several cats in one study that were initially treated conservatively subsequently required surgery because of worsening clinical signs (Basher and Fowler, 1987). Conservative management is not described in the dog; most linear foreign bodies in dogs are lodged in the pylorus and, since 40% of dogs reportedly have peritonitis at the time of surgery, immediate surgical intervention is recommended.

Delay in surgical removal may result in serious morbidity because of development of perforations, peritonitis and sepsis; therefore, surgical removal of linear foreign bodies is considered the safest treatment for most animals. At laparotomy, the foreign body is typically removed through multiple enterotomies (see Figure 12.8). An enterotomy incision is made midway along the site of the obstruction and the string is located and grasped. The anchored portion under the tongue or in the pylorus can then be cut without losing control of the foreign body. The foreign body is gently retracted to remove as much as possible. Removal of its entire length may, however, require multiple enterotomies. It is important not to pull too vigorously on the foreign body, as this may cause perforation of an already compromised intestinal wall. Perforations of the mesenteric border of the plicated bowel may not become apparent until the tension on the string is released and the plications relax. Even then, this area of the bowel can be difficult to evaluate due to the presence of mesenteric fat. Large sections of the intestine may have multiple mesenteric perforations, necessitating resection.

A single enterotomy catheter technique has been described in cats. A 1 cm incision is made in the antimesenteric border of the proximal duodenum. The foreign body is grasped through this incision, cut at its anchor point, and then tied to a segment of rubber or silicone catheter or tubing. The catheter is inserted distally into the intestines with the attached string, and the enterotomy is closed. The catheter is then milked aborally through the intestines and out to the anal orifice, carrying the foreign body with it. Because linear foreign bodies in dogs tend to be wider in diameter (i.e. fabric, carpet, plastic, tights), it is unlikely that this technique would be useful in this species.

The prognosis following uncomplicated linear foreign body removal in cats is good. Intestinal perforations, which are uncommon in cats, are more likely to be associated with death after surgery. The prognosis for dogs is more guarded. The probability of peritonitis and death is nearly double that reported in cats.

Intussusception

An intussusception is the invagination of one portion of the gastrointestinal tract into the lumen of an adjoining segment. Affected animals are often less than a year of age. The condition may be associated with enteritis secondary to parasites, viruses, linear foreign bodies, intestinal masses or previous abdominal surgery; in older animals, it is often associated with neoplasia.

The clinical signs are those of bowel obstruction, including vomiting, diarrhoea, depression and anorexia. Clinical signs vary with the level and completeness of the obstruction. Animals with duodenojejunal and proximal jejunal intussusception often have frequent vomiting. Animals with ileocolic intussusception vomit less frequently and may have a more chronic history of tenesmus and haematochezia.

In affected dogs, a cylindrical mass in the cranial to mid-abdomen is often palpable. On plain radiographs, a mass effect or accumulation of gas proximal to the intussusception may be noted. Intussusception can be differentiated from other causes of intestinal obstruction with contrast studies or ultrasonography. On ultrasonography, an intussus-ception appears as a series of concentric rings in the transverse image or parallel lines in a longitudinal image, reflecting the folded layers of the intestinal wall (see Chapter 24).

Surgical reduction or resection is usually required to correct intussusceptions. During surgery, the entire gastrointestinal tract is carefully examined, since multiple intussusceptions can occur simultaneously. Manual reduction can be attempted if the visible enteric vessels are patent and the bowel wall does not look ischaemic. Resection and anastomosis (see Figure 12.9) is required when the lesion cannot be reduced, the involved bowel is necrotic, or underlying neoplasia is suspected.

After surgery, animals should be tested and treated for endoparasites and any underlying predisposing conditions (i.e. viral enteritis). Prognosis for animals that have received appropriate supportive care and have undergone uncomplicated reduction or resection of small intestinal intussusception is good. Recurrence rates range from 6 to 27%. Recurrences are usually noted within 3 days but have been reported up to 3 weeks after surgery. Enteroplication (see Figure 12.8) to reduce the recurrence rate is controversial. One study (Oates *et al*., 1994) documents decreased intussusception recurrence with enteroplication but other case reports suggest enteroplication can cause serious complications in some animals (Kyles *et al*., 1998).

Mesenteric volvulus

Mesenteric volvulus is a rare and usually fatal condition in which the bowel twists on its mesenteric axis, resulting in strangulating mechanical obstruction of the small intestines and compression of the cranial mesenteric artery and its branches. With a mesenteric volvulus, the thin-walled veins and lymphatics become obstructed first, resulting in oedema formation and vascular engorgement of the bowel wall. Eventually, the cranial mesenteric artery and its branches are obstructed, leading to ischaemic necrosis of the distal duodenum, jejunum, ileum, caecum, ascending colon and proximal descending colon.

The cause of mesenteric volvulus is unknown, although it has been reported in association with other diseases, including lymphocytic plasmacytic enteritis, ileocolic carcinoma, gastrointestinal foreign bodies, recent gastrointestinal surgery, blunt abdominal trauma, GDV, and exocrine pancreatic insufficiency. The disease tends to occur in young adult, male, large-breed dogs. German Shepherd dogs and possibly English Pointers may be predisposed. It has also been reported in a cat.

Clinical signs are peracute to acute, with rapidly progressive abdominal distention and haematochezia reported most frequently. Vomiting secondary to obstruction and pain has also been reported in some animals. The diagnosis can be challenging because the clinical signs are non-specific and the condition is rapidly progressive. In general, if an animal presents in shock with gaseous abdominal distension that is not relieved by appropriate placement of an orogastric tube, mesenteric volvulus should be suspected and surgery, if it is to be performed, should not be delayed by diagnostic tests.

Abdominal radiographs may initially be unremarkable. With progression of the disease, gaseous distension of the entire intestinal tract is noted. The stomach and descending colon are usually not dilated. The uniform and extensive nature of the small intestinal distension and normal position of the stomach help differentiate this condition from a simple mechanical obstruction of the small bowel or a GDV. Unfortunately, once the diagnosis becomes clear on radiographs, most of the intestinal tract is often ischaemic and necrotic, and the animals are destined to die or be euthanased. Derotation and reoxygenation of the bowel may actually increase the severity of the systemic response through reperfusion injury.

Unless recognition and treatment of the condition are immediate or the volvulus is only partial, prognosis for recovery is grave. The vast majority of dogs succumb to the cascade of vascular obstruction, intestinal ischaemia, and circulatory, endotoxic and cardiogenic shock (Figure 12.10).

Trauma

Penetrating abdominal injury may cause direct perforation of the bowel. Blunt trauma may result in acute intestinal tears or in ischaemic necrosis and eventual perforation secondary to vascular compromise. Both types of trauma may lead to development of septic peritonitis; however, in cases of blunt trauma, the diagnosis is often delayed for several days.

Volvulus	Surgical intervention	Prognosis
Gastric	• Derotation of the stomach • Resection of non-viable stomach • Splenectomy if necessary • Gastropexy	Good
Splenic	• Splenectomy • The twisted organ pedicle should not be untwisted prior to resection • Prophylactic gastropexy in the stable patient	Good
Liver lobe	• Liver lobectomy • The twisted organ pedicle should not be untwisted prior to resection	Good
Mesenteric	• Intraoperative euthanasia is usually indicated due to extensive bowel necrosis • Derotation may be performed in the rare case that the bowel is not completely necrotic	Grave
Caecocolic	• Replacement of the bowel into its normal location • Resection of non-viable tissue • Colopexy	Guarded

12.10 Types of abdominal organ volvulus necessitating emergency surgical intervention.

Clinical signs may include abdominal pain, vomiting, bloody stools, lethargy, anorexia or shock. Clinical findings and results of bloodwork are not good predictors of intraperitoneal injury. Blunt probing of the wound can also be inaccurate. On abdominal radiographs, animals with a penetrating gastrointestinal wound may have free gas within the abdominal cavity, either entering through the wound or leaking from perforated intestine if the omentum did not seal the leak. Analysis of fluid obtained by abdominal paracentesis and/or lavage is important for early recognition of intra-abdominal injury. If an adequate amount of fluid cannot be obtained by paracentesis, peritoneal lavage should be performed. Exploratory laparotomy is indicated if bacteria or vegetative matter are seen on cytology, or if neutrophils are degenerate and significantly increased in number. If results of abdominal fluid cytology are normal but intestinal damage is still a concern, radiographs and peritoneal lavage can be repeated at a later time, or an exploratory laparotomy can be performed.

The surgical management of small bowel perforations depends on the size, location and number of perforations, as well as the vascular supply to the involved bowel segment(s). Small defects in an otherwise healthy segment of bowel may be amenable to debridement and primary closure (see Figure 12.8). Large defects or those involving non-viable bowel segments require intestinal resection and anastomosis. Prognosis for traumatic intestinal wounds depends largely on the duration and extent of damage.

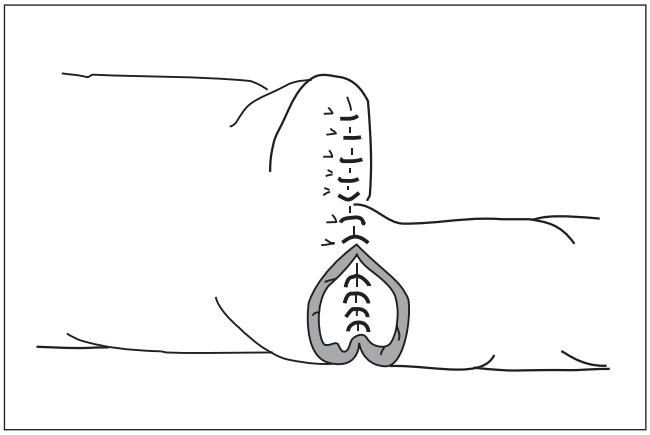
Postoperative management following intestinal surgery

An acute awareness of the possible complications of small intestinal surgery is required in order to manage these patients successfully. Postoperative complications can be relatively minor, such as anorexia or mild regurgitation, or severe, including aspiration pneumonia and septic peritonitis. Any animal that develops worsening vomiting, abdominal pain or fever following intestinal surgery should be evaluated for dehiscence of the intestinal surgical site (see Peritonitis, below). Risk factors for dehiscence include inadequate resection of compromised intestine, presence of systemic inflammatory response, presence of septic peritonitis and hypoalbuminaemia. Attention to fluid balance and analgesia is important as for any postsurgical patient. Some animals, especially those that remain anorexic, those with extensive bowel resections, or those that require aggressive fluid resuscitation, will become hypoalbuminaemic and may require colloidal support. It is especially important to maintain enteral nutrition in these patients, as adequate nutrition of enterocytes can occur only from the lumen of the intestine – failure to adequately address nutritional deficiencies will lead to reduced wound healing and a higher risk of dehiscence. Partial enteral feeding can usually be easily achieved by placement of a nasogastric or naso-oesophageal feeding tube. Some patients will develop ileus following small intestinal surgery, which can cause vomiting and regurgitation. In addition to antiemetics, pro-motility agents such as metoclopramide or erythromycin can be used to promote intestinal motility and make these patients more tolerant of enteral feeding. Typically, if the surgery was undertaken without significant contamination and there is no evidence of peritonitis, antimicrobial treatment is not indicated beyond the perioperative period.

Large intestine

Intussusception

Severe colonic obstruction can occur secondary to intussusception. On plain radiographs, a mass effect or accumulation of gas proximal to the intussusception may be noted. Confirmation of the diagnosis through a contrast study is most quickly attained via a barium enema. Surgical treatment involves reducing the intussusception. In situations where this is not possible, the affected area of bowel is resected and the ends anastomosed (see Figure 12.8). This often involves resection of the ileum and anastomosing a jejunal segment of bowel to a colonic segment of bowel (Figure 12.11).



12.11 Diagrammatic representation of anastomosis of the small intestine to the large intestine. The large intestine has been oversewn so that its lumen approximates the size of the small intestine. The front is still to be sutured.

Caecocolic volvulus

Caecocolic volvulus has been reported infrequently in both dogs and cats. Clinical signs include vomiting, tenesmus, diarrhoea and shock. Radiographs reveal severely dilated loops of bowel in the caudal abdomen. Surgery involves replacement of the bowel in its normal location and resection of non-viable tissue. Colopexy (see Figure 12.8) may prevent recurrence. The prognosis for this condition is guarded, as at least 50% of the animals reported with this condition died in spite of intensive treatment (see Figure 12.10).

Perforation

Perforation of the colon is a true emergency because of the high colonic bacterial content. Untreated, colonic perforations are rapidly fatal. Perforation occurs secondary to penetrating trauma, rupture of colonic neoplasms or, rarely, from foreign bodies. Leakage may also be seen at biopsy sites following surgical biopsy of the colon. Due to the high colonic bacterial load and consequences of biopsy site leakage, full-thickness colon biopsies should be undertaken only if absolutely necessary. Perforation has also been associated with corticosteroid administration in animals with intervertebral disc prolapse.

The diagnosis is initially one of peritonitis, based on the clinical signs of shock, abdominal distension and pain, and confirmed by a peritoneal tap or lavage showing severe peritonitis, with degenerate neutrophils and intracellular bacteria. Emergency fluid resuscitation, antibiotics and laparotomy are indicated. At surgery, the affected area of colon is packed off and either debrided and sutured or resected. Treatment for peritonitis is discussed later in this chapter.

Rectal prolapse

Rectal prolapse occurs in young, unthrifty parasitized animals, in association with tumours and following perineal hernia repairs. Clinical signs are obvious; however, it is necessary to distinguish prolapse of the anus and colon from intussusception of ileum.

The prolapse must be amputated if it is necrotic. In other cases the prolapsed rectum is reduced. The oedema is removed by gentle pressure and massage using a soft cloth moistened with warm saline. Following reduction, a loose purse-string suture is inserted in the anus. This is removed in 3–5 days. In cases where the prolapse reoccurs, colopexy is indicated. A caudal, ventral midline laparotomy is performed. Gentle cranial traction is placed on the descending colon whilst an assistant reduces the rectal prolapse. The descending colon is sutured to the abdominal wall by a double row of sutures.

Postoperative care following surgery of the large intestine

Surgery of the large intestine has potentially serious complications. A high index of suspicion for leakage is required because if not caught early, this is almost uniformly fatal. These patients can appear septic and require extensive antimicrobial, fluid and sometimes vasopressor support. The crystalloid fluid requirements of these patients can be quite high due to significant loss of fluid into the colon. Other postoperative care is standard as for all intestinal surgeries (see above). Successful treatment relies on treatment of the underlying condition (often parasites).

There is no evidence that postoperative antibiotics improve colon healing or decrease the incidence of postoperative infection. However, postoperative antibiotics are indicated in cases where contamination or colonic perforation is discovered at surgery. Parenteral antibiotics are required, and broad-spectrum antimicrobials with efficacy against anaerobes are indicated. Examples would include a second-generation cephalosporin (e.g. cefoxitin) or a penicillin combined with a fluoroquinolone and metronidazole. Bacterial translocation across a compromised colonic wall does occur, especially in dogs with diseases with extensive colonic involvement, such as a colonic volvulus.

Pancreas

Emergency surgery of the pancreas is usually limited to abscess drainage or removal. Abscesses are diagnosed by ultrasonographic evaluation of the pancreas. They appear as large, hypoechoic areas within the inflamed pancreas. Aspiration of pus from a cavity within the pancreas is an indication for surgical exploration. The surgeon should be thoroughly familiar with the anatomy of the pancreas, its blood supply, and the pancreatic and common bile ducts to avoid damaging vessels supplying the duodenum and stomach, the pancreatic papillae or the common bile duct. If the abscess is thick-walled and well delineated, it may be treated by closed-suction drainage. A balloon catheter (such as a Foley) is placed through the body wall and into the abscess cavity. The abscess cavity is thoroughly

drained and flushed repeatedly at surgery. The abscess is then drained for 5–10 days postoperatively. Alternatively, the affected area of the pancreas is opened, debrided and flushed. Omentum is then packed into the cavity. The surgeon should strongly consider placing a jejunostomy tube to allow for postoperative enteral nutrition. This measure is controversial in human medicine and controlled clinical trials of its use in veterinary medicine are lacking. How-ever, one author [DEH] has had some success with its clinical use. The abdomen is generously lavaged with warm, balanced electrolyte solution. Open peritoneal drainage is considered in cases that have severe peritonitis associated with the pancreatitis (see Peritonitis below).

Postoperative management following pancreatic surgery

In addition to standard care for gastrointestinal surgery patients as described above, pancreatitis cases require special attention to analgesia and nutrition postoperatively. Postoperative pain can be severe if significant pancreatitis is present, and use of adjunct techniques and medications such as local blocks, epidural anesthesia or 'add-on' medications such as lidocaine (25–50 μg/kg/min) or ketamine (5–10 μg/kg/min) can help to reduce the requirement for opioids.

Nutrition is crucial in the recovery of these patients. Since the goal of minimizing stimulation of the pancreas may make it impossible to feed the patient through an oesophagostomy or gastrostomy tube placed at surgery, enteral feeding can be accomplished via a jejunostomy tube. Total parenteral nutrition (TPN) (see Chapter 22) can be considered if complete enteral feeding is not tolerated or a jejunostomy tube is not available. Although this provides the calories and nutrients for recovery, it lacks the ability to nourish the enterocytes. If possible, a small amount (10% of resting energy expenditure) of food should be provided enterally concurrent with the TPN.

The output from the peritoneal drain, if used, should be monitored. If the drainage volume increases, or the fluid character or cytological examination worsens (e.g. an increase in nucleated cell count, more degenerate neutrophils or intracellular bacteria), then the clinician should be concerned about development of septic peritonitis or progressive necrosis, which may require re-exploration of the abdomen via a second laparotomy. Broad-spectrum antimicrobials should be administered in cases of pancreatic abscess pending culture and sensitivity results (see Peritonitis).

Biliary surgery

True surgical emergencies of the biliary tract are usually associated with leakage of bile, which can occur secondary to trauma, cholelithiasis or gall bladder infarction. Penetrating trauma (gunshot, arrow or stabbing wounds) can damage any part of the biliary system and cause leakage from hepatic ducts, the common bile duct or the gall bladder. Choleliths generally cause biliary obstruction, but can occasionally perforate the common bile duct. Gall bladder infarction has been seen in dogs with increasing frequency in recent years. The gall bladder undergoes transmural coagulative necrosis with minimal associated inflammation. In some cases, thrombi are found in vessels supplying the gall bladder. This condition has been associated with underlying diseases including hypothyroidism and hyperadrenocorticism, and has been seen in conjunction with biliary mucoceles and occasionally choleliths.

Clinical signs are variable and depend somewhat on the underlying cause of the disease. In cases of biliary leakage secondary to trauma, the clinical signs may reflect bile peritonitis or may be associated with other injuries caused by the inciting trauma, such as severe haemorrhage or bowel perforation. Animals with cholelithiasis and gall bladder necrosis frequently have non-specific clinical signs including vomiting, anorexia and diarrhoea. Icterus is not a consistent clinical sign. Serum liver enzymes and bilirubin are often variably elevated. Plain abdominal radiographs show a loss of detail in the cranial abdomen and may reveal radiopaque choleliths. Abdominal ultrasonography allows visualization of the liver and gall bladder, and allows the clinician to sample and subsequently analyse small amounts of peritoneal effusion. Bilirubin levels that are higher in peritoneal fluid than in the serum are an indication for exploratory laparotomy.

Stabilization of the animal with bile peritonitis is discussed in more detail in the Peritonitis section. Evaluation of a preoperative coagulation screen is mandatory, as the absence of bile in the digestive tract prevents adequate emulsification of dietary fats and the absorption of fat-soluble vitamins, including vitamin K. Although it may seem logical that many animals with biliary obstruction or bile leakage would be hypocoagulable, a recent study using thromboelastography indicates that many dogs are hypercoagulable (Mayhew *et al*., 2013). The implications of this study for case management are not clear. Traditionally, vitamin K supplementation has been administered; the authors have had no experience of heparinizing animals requiring biliary surgery, although they would recommend waiting until after surgery if possible.

At surgery, a complete exploratory laparotomy is performed. Careful evaluation of each liver lobe, the hepatic and common bile ducts, and the gall bladder is vital, although often made difficult by omental and visceral adhesions. Rupture of a hepatic duct is managed by ligating the duct; collateral drainage of bile from the affected liver lobe will develop. Choleliths that have perforated the common bile duct are removed. Often, the opening in the common bile duct must be enlarged to facilitate removal. The duct is then sutured closed with fine (0.7 or 1 metric (6/0 or 5/0 USP)) synthetic absorbable suture material over a stent placed through the major duodenal papilla and passing retrograde up the common bile duct. If suturing the duct is not possible or results in duct stenosis, the common bile duct is ligated proximal to the leaking area and a cholecystoduodenostomy or jejunostomy is performed. In cases of necrotizing cholecystitis, the duodenum is opened and the common bile duct is catheterized and flushed to ensure patency of the biliary tree. The gall bladder is then dissected free of the right medial and quadrate liver lobes, the cystic duct and artery are ligated using transfixation sutures, and the gall bladder is removed.

Postoperative management following biliary surgery

Postoperative management consists of standard supportive care. Serial evaluations of blood chemistry should reveal normalization of bilirubin, cholesterol and liver values. An increase in these values or worsening of the patient's condition should prompt investigation for dehiscence and subsequent bile peritonitis (see Peritonitis), obstruction of the biliary tract, or other complications such as aspiration pneumonia.

Peritonitis

The peritoneum is a serous membrane lining the abdominal cavity and reflecting around the abdominal organs. In the normal animal, a small amount of fluid separates the parietal and visceral peritoneal layers and decreases friction between the abdominal contents. Fluid in the peritoneal space drains via diaphragmatic lymphatics to sternal and mediastinal lymph nodes and the thoracic duct. Pathological fluid (or contamination) disperses rapidly throughout the peritoneal cavity.

Peritonitis is defined as any inflammatory process involving the peritoneum. In most cases, peritonitis occurs as a sequela of another disease process, and can be aseptic or septic. Aseptic peritonitis may be secondary to foreign bodies (surgical sponges), ruptured neoplasms, or chemical agents such as pancreatic enzymes, bile or urine (although these can contain bacteria), and stomach or proximal duodenal contents in dogs, in which bacterial concentrations are low. Primary peritonitis occurs most commonly in cats, especially those with coronavirus infection and feline infectious peritonitis.

Septic peritonitis results from stomach or bowel perforation, penetrating wounds, surgical contamination, or extension of a urogenital infection (ruptured pyometra or prostatic abscess). The peritoneum is exposed to large numbers of anaerobic and Gram-negative organisms as well as chemical bowel contents. Endotoxin is liberated and produced as bacteria grow in the peritoneal exudate.

Chemical injury results in inflammation of the peritoneum. Vasodilatation and increased vascular permeability initially result in loss of isotonic fluid into the peritoneal cavity. As vascular permeability increases, albumin is lost into the peritoneal space. Given the large peritoneal surface area, fluid and protein loss can be massive. Diaphragmatic lymphatics, which normally return peritoneal fluid to the systemic circulation, become overloaded and plugged with fibrin. Concurrent vomiting and diarrhoea exacerbate fluid loss. Fluid loss decreases circulating blood volume and results in decreased cardiac output and poor tissue perfusion, which in turn results in cellular hypoxia and anaerobic cellular metabolism. Cellular energy depletion causes loss of cell membrane integrity, cell death and eventually organ failure.

Different aetiological agents cause some variation in the pathophysiology of chemical peritonitis. For example, uroperitoneum rapidly causes a life-threatening hyperkalaemia, which if present should be initially treated by aggressive fluid resuscitation and a slow intravenous injection of calcium gluconate (a functional antagonist of potassium) at a dose of 50 mg/kg. Although it does not lower serum potassium, calcium returns membrane excitability to normal for approximately 20–30 minutes. Regular insulin (0.2 (or 0.25)–0.5 IU/kg) and glucose (1–2 g/IU of insulin) can also be administered intravenously if the animal has symptomatic hyperkalaemia (see Chapter 5). Animals with uroperitoneum often have severe metabolic acidosis. Sodium bicarbonate can be administered (1–2 mmol/kg i.v.) to correct acidosis (see Chapter 5). Bile, although usually sterile, can cause permeability changes in the intestinal wall, allowing transmural bacterial migration. Gastric and pancreatic secretions are more irritating than bile, and produce a rapid and severe peritonitis.

In animals with septic peritonitis, bacteria are initially rapidly opsonized by white blood cells or absorbed by diaphragmatic lymphatics. Haemoglobin and mucus enhance the virulence of intraperitoneal organisms. Bacterial synergism, wherein the virulence of the total bacterial load is greater than the sum of the individual organisms, occurs. Bacterial destruction liberates endotoxins, exotoxins and proteases. Endotoxin and cell membrane damage both activate the arachidonic acid pathways, generating prostaglandins and leukotrienes. The complement, clotting and fibrinolytic systems are also activated. Macrophages are stimulated to release tumour necrosis factor, which triggers the release of other inflammatory cytokines. Ongoing absorption of bacteria and toxins and generation of inflammatory mediators results in generalized sepsis or the systemic inflammatory response syndrome (SIRS).

Systemically, the animal responds to these profound changes by attempting to maintain perfusion to the heart and brain. Hypotension stimulates the carotid baroreceptors; subsequent inhibition of vagal tone and sympathetic stimulation should increase heart rate and cause peripheral vasoconstriction. In practice, many animals with peritonitis have at least a phase of peripheral vasodilatation due to SIRS. This occurs for several reasons, including decreased vasopressin levels, increased nitric oxide synthesis and opening of cellular potassium channels, secondary to a lack of adenosine triphosphate, acidosis and increased cellular lactate concentrations. Opening of cellular potassium channels allows potassium to escape from the smooth muscle cells of the arterial walls, hyperpolarizing them and preventing vasoconstriction.

Peritonitis is often difficult to diagnose. The clinical signs are largely non-specific. Depression and diffuse abdominal pain are often present, to a degree greater than that usually seen following abdominal surgery or trauma. Some animals splint their abdominal wall in response to palpation. Vomiting is also a prominent sign of peritonitis. In addition to the effusion, peritoneal inflammation often causes a paralytic ileus and intestinal dilatation.

In septic peritonitis, fever and leukocytosis are not consistent findings. Animals with peritonitis may have a leukocytosis with a left shift, or a neutropenia. In uroperitoneum, elevations in blood urea nitrogen (BUN), serum creatinine and potassium are often detected; however, in early cases these values can all be normal. Serum alkaline phosphatase, alanine aminotransferase and total bilirubin levels are usually elevated in cases of bile peritonitis. Abdominal radiographs may show free gas or a lack of intestinal detail and a ground glass appearance from free fluid in the abdominal cavity. Recovery and examination of peritoneal exudate is extremely valuable in the diagnosis of peritonitis. Abdominocentesis is ideally performed with ultrasound guidance, and if this does not yield fluid, peritoneal lavage should be considered. This technique and results of cell counts in dogs after abdominal surgery are discussed earlier in this chapter. Degenerate neutrophils with intracellular bacteria indicate septic peritonitis. Creatinine, potassium and bilirubin levels may also be measured in the peritoneal fluid.

A low peritoneal fluid glucose concentration (2.8 mmol/l) and a high peritoneal lactate concentration (>5.5 mmol/l) have been reported to be specific indicators of septic peritonitis in veterinary patients (Swann and Hughes, 2003). In a more recent study, peripheral blood and peritoneal fluid glucose and lactate concentrations were compared (Bonczynski *et al*., 2003). Peritoneal fluid glucose concentrations that were 1.1 mmol/l lower than those in the serum, and peritoneal lactate concentrations 2 mmol/l higher than those in the peripheral blood, were 100% sensitive and specific for a diagnosis of septic peritonitis in dogs.

These guidelines unfortunately do not apply to animals that have had recent abdominal surgery. In these animals, postoperative peritoneal fluid and lactate levels must be

interpreted with caution, as values compatible with peritonitis have been seen, in peritoneal fluid obtained from healthy dogs following laparotomy. In these cases, detailed analysis of cytology and following trends in neutrophil appearance and peritoneal fluid cell count can be helpful.

Aggressive patient stabilization is required prior to anaesthesia and surgery. Intravenous fluids are administered to restore perfusion, typically initially isotonic crystalloids in sequential intravenous boluses of 20–30 ml/kg until normalization of cardiovascular parameters occurs, up to a dose of 90 ml/kg. Capillary refill time, heart rate, arterial blood pressure, urine output, lactate clearance and central venous pressure are monitored to assess the response to therapy. Plasma or synthetic colloids (hydroxyethyl starches, dextran 70) may be required because of the massive loss of albumin into the peritoneal cavity (a more detailed discussion of decision making in regard to fluid therapy, can be found in Chapter 4). The choice of fluid type and electrolyte supplementation is based on the results of sequential electrolyte and blood gas measurements.

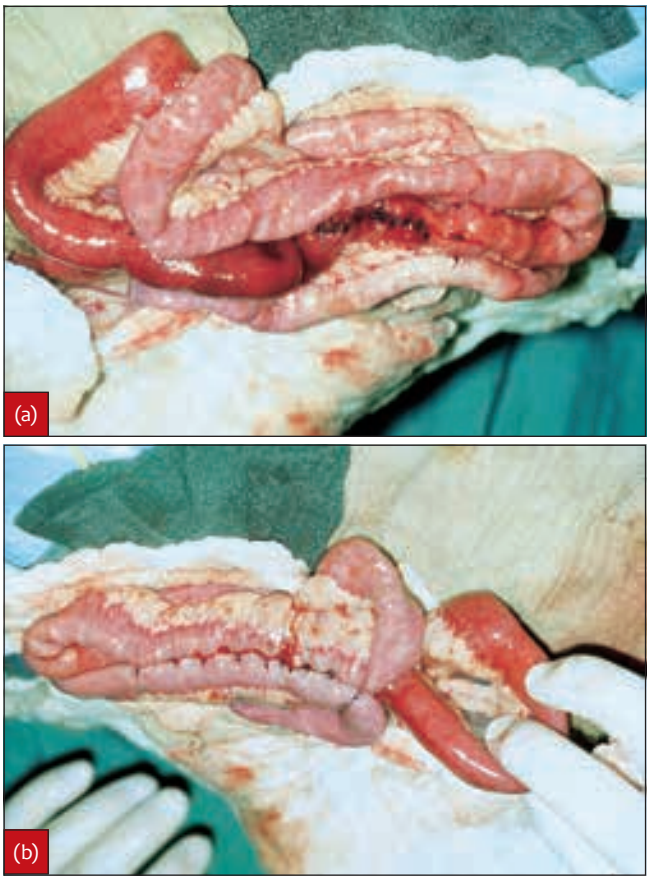
Broad-spectrum, bactericidal antibiotics are administered intravenously as soon as the diagnosis of peritonitis is made. Antibiotics effective against Gram-positive and -negative, aerobic and anaerobic bacteria are recommended. A combination of a potentiated penicillin with an aminoglycoside or fluoroquinolone antibiotic is usually effective, although a study in the USA demonstrated a high rate of community acquired enrofloxacin resistance in *Escherichia coli* (Falagas *et al*., 2007). Alternatively, a regular penicillin or first-generation cephalosporin such as ampicillin or cefazolin can be combined with a fluoroquinolone or amikacin, to provide similar broad spectrum coverage. If a regular (as opposed to potentiated) penicillin is used then metronidazole should be added to the regime to improve cover for *Bacteroides* sp.; this is especially important in cats. Cefazolin (20 mg/kg i.v. q6h) should be used in preference to cefalotin, which does not reach adequate tissue levels in dogs. In euvolaemic animals without renal disease, amikacin should be administered once daily at 15 mg/kg i.v. as the single high dose is more effective and less nephrotoxic than multiple smaller doses. Enrofloxacin should also be administered at the high end of the dose range once daily, making it less suitable for use in cats with septic peritonitis due to its potential for ocular toxicity. Penicillins, cephalosporins and aminoglycosides all reach intraperitoneal levels equivalent to their serum levels. In patients with hospital-acquired septic peritonitis, it is especially important to be aware of the possibility that resistant Gram-negative organisms might be present. In this case a potentiated penicillin with an aminoglycoside is an excellent choice, although resistance patterns vary widely based on geography and hospital type.

High-dose corticosteroid administration in septic shock has largely been abandoned after human clinical trials showed that corticosteroids were associated with a higher mortality. However, a subset of patients with peritonitis and refractory septic shock requiring vasopressor therapy may have poor adrenal function. These patients may benefit from physiological doses of glucocorticoids and mineralocorticoids; typically, hydrocortisone at 0.5 mg/kg i.v. q6h or 2 mg/kg/day as a constant rate infusion (CRI) is recommended (see Chapter 3). NSAIDs are rarely used in dogs with septic peritonitis. Despite some theoretical benefits of reducing the inflammatory response in sepsis, the risk of severe side effects associated with use of NSAIDs in dogs and especially cats with compromised renal and gastrointestinal perfusion likely outweighs the benefits.

One of the most important aspects of treating peritonitis is prompt removal of the inciting cause. While the animal should be stabilized before anaesthesia and surgery, the underlying source must be addressed to resolve the peritonitis. Exploratory laparotomy is mandatory to treat the source of the peritonitis, remove peritoneal contamination and exudate, and provide a route for enteral nutrition. A large ventral midline incision is used for exposure. A complete exploratory laparotomy is performed. The source of the peritonitis is identified and isolated from the remainder of the abdomen using moistened laparotomy sponges. In animals with generalized peritoneal contamination, the authors prefer to lavage the peritoneal cavity with a large volume of warm sterile saline before proceeding with definitive treatment. The fluid is immediately aspirated from the peritoneal cavity.

Definitive treatment of peritonitis often involves resection and anastomosis of damaged bowel. Omental wrapping or serosal patching is recommended to reinforce anastomoses in the face of peritonitis. Serosal patching is a technique in which loops of healthy bowel are loosely sutured to the bowel adjacent to the anastomosis (Figure 12.12). The serosal surfaces of the healthy bowel are then in contact with the anastomosis site, allowing a reinforcing fibrin seal to form.

Few animals with peritonitis will eat voluntarily, and many vomit during the postoperative period, so mechanisms for nutritional support should be considered during



12.12 Serosal patching. (a) Two healthy loops of small intestine are brought alongside the loop of bowel to be patched. Sutures are placed between the mesenteric side of the normal and affected intestine loops. (b) The antimesenteric surfaces of the two healthy loops of intestine are apposed with single interrupted sutures, covering the affected area with bowel. Note: this procedure should only be performed to reinforce healthy bowel. Patching does not remove the need for accurate assessment of bowel viability and resection of unhealthy bowel.

surgery. Placement of an oesophagostomy, gastrostomy or jejunostomy tube should be considered unless it interferes with repair of the leaking intestine.

The peritoneal cavity should be thoroughly lavaged with a large volume of warm, sterile, balanced electrolyte solution to remove bacteria and debris. The volume of fluid required varies from 500 ml in a cat to several litres in a large dog. All lavage fluid must be aspirated. Lavage with inadequate aspiration merely spreads bacteria throughout the peritoneal cavity, and sequesters them from phagocytosis.

The addition of antiseptics to the lavage fluid has been controversial, and is currently not recommended. Several human studies have concluded that there is no benefit to adding povidone–iodine to lavage fluid. Experimental studies have shown that 2 ml/kg of povidone–iodine (10% solution, 1% available iodine) instilled into the peritoneal cavity of dogs with peritonitis is lethal (Bolton *et al*., 1975). Intraperitoneal povidone–iodine also decreases the neutrophil percentage and increases bacterial numbers in the peritoneal cavity in rats with experimental peritonitis. The addition of antibiotics to peritoneal lavage fluid is also debated. Most studies indicate that this treatment is not beneficial in patients receiving appropriate parenteral antibiosis (Gerding, 1977).

Contamination often remains within the peritoneal cavity even after extensive debridement and lavage. The veterinary surgeon must decide which cases require postoperative peritoneal drainage. Local peritoneal drainage is important when the inflammation is confined to a specific area of the peritoneal cavity. Drainage tubes, with or without suction, can be used in such cases; examples include prostatic and pancreatic abscesses. Ideally, drain exit points should be covered with a sterile dressing. Drainage tubes were, until recently, considered ineffective for draining the entire peritoneal cavity, as they were thought to be rapidly sealed by fibrin and omentum. The presence of drains, which are effectively foreign bodies, resulted in increased bacterial translocation and histological inflammation in an experimental peritonitis model. In spite of this experimental data, draining the peritoneal cavity with closed suction drains has been described in clinical cases of peritonitis in dogs and cats, with similar results to open drainage (Mueller *et al*., 2001). Drains are placed in the cranial, and sometimes caudal, abdomen (Figure 12.13). Use of closed suction drains is increasingly replacing open peritoneal drainage as the technique of choice for managing postoperative peritonitis patients.



12.13 Two closed suction drains, one placed in the cranial abdomen and one placed in the caudal abdomen, used to drain the peritoneal cavity after surgery for septic peritonitis.

Open peritoneal drainage is accomplished by incompletely closing the abdominal incision. The falciform ligament is removed, and the linea alba is sutured with a continuous monofilament suture leaving a gap of 2–4 cm between the wound edges (Figure 12.14). The wound is bandaged using a sterile dressing of Vaseline-impregnated gauze covered by sterile towels. This primary dressing is covered with a layer of thick, absorbent material, a layer of conforming, stretchable gauze bandage, then adhesive tape. The dressing usually needs to be changed every 6 hours initially, as fluid from the peritoneum soaks through. Bandage changes are performed under sterile conditions with the animal sedated. Fibrinous adhesions, which may entrap peritoneal exudate, are gently freed. There are no exact criteria to help the clinician judge either which cases of peritonitis require open abdominal drainage, or when to close the open incision. In general, the incision is closed when drainage has decreased and the peritoneum appears grossly healthy at bandage changes. This generally occurs 3–5 days after the initial surgery. Closure should be performed as a complete laparotomy, and the peritoneal cavity examined for any evidence of residual infection. In cases of severe generalized peritonitis, a 'second look' surgery can be performed 24–48 hours after the initial laparotomy; this serves to allow re-flushing of the abdomen, to inspect the surgical site and to re-evaluate tissue viability in a more stable patient setting. A repeat laparotomy is rarely performed but is potentially an alternative to open abdominal management.



12.14 Open peritoneal drainage. The linea alba is sutured approximately 3 cm apart with non-absorbable material. This open incision is then covered with a sterile bandage that will require changing every 6–12 hours.

Postoperative management of peritonitis

Patients recovering from septic peritonitis can recover routinely or can be amongst the most challenging of critical care patients. Postoperative mortality rates can be as high as 45%, often due to recurrence of peritonitis or organ failure.

Dehiscence of intestinal surgical sites and subsequent recurrence of peritonitis is not uncommon, with the risk of dehiscence increased by the debilitated state of the patient and the inflammatory peritonitis impairing wound healing. A change in the patient's status should prompt immediate assessment for dehiscence. Abdominal fluid should be examined daily for cell counts and cytology – this is ideally done by direct paracentesis as use of fluid from a contaminated drain can give a false impression of recurrent sepsis.

Fluid and albumin losses can be extensive, particularly in patients with open peritoneal drainage. Intravenous fluid therapy must be optimized to keep up with the ongoing losses, in order to maintain tissue perfusion.

Additional complications can include aspiration pneumonia and thromboembolic disease. Coagulation testing should be performed, and abnormalities treated with blood products if needed. Respiratory status must be monitored and oxygen provided if hypoxia is present. Antiemetics and gastrointestinal protectant drugs are usually required. Nutritional support is crucial (see Postoperative management following intestinal surgery, above) to support healthy enterocyte growth during what can be a prolonged recovery. Broad-spectrum aggressive antimicrobials should be continued until culture and sensitivity results are available. At this point the antimicrobial regime may be reduced if appropriate. The reader is directed elsewhere in this book for a detailed discussion of critical care, respiratory and cardiovascular monitoring, and support (see Chapters 3, 4, 5, 6, 7, 22 and 25).

Haemoperitoneum

Haemoperitoneum is the abnormal accumulation of blood in the peritoneal space and is a common diagnosis in small animal emergency practice. Neoplasia, ruptured splenic haematomas, and trauma are the most common causes of haemoperitoneum. Definitive diagnosis is made by retrieval of a sample of the peritoneal fluid for analysis. Abdominocentesis using 'blind' or ultrasound-guided techniques will reveal a sanguineous non-clotting peritoneal fluid. If the blood retrieved by abdominocentesis forms clots, inadvertent splenic or vascular penetration should be suspected.

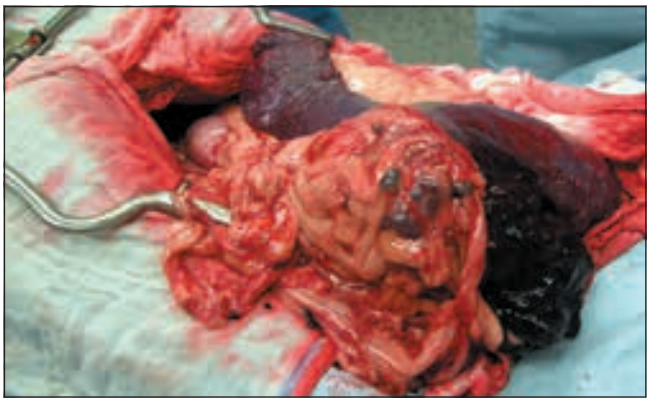
Regardless of the cause of haemoperitoneum, circulatory support is often required for stabilization. The rate and composition of intravenous fluids is tailored to each individual animal, and PRBCs or whole blood transfusions may be required. Preoperative resuscitation should aim to maintain or increase the PCV to at least 25% without increasing systolic blood pressure above 90 mmHg or the mean arterial pressure above 65 mmHg. In an experimental haemorrhage model (Sondeen *et al*., 2003), increasing systolic pressure above 90 mmHg resulted in re-haemorrhage. Several strategies are available for use; in all of these strategies the aim is to resuscitate the patient preoperatively 'just enough', but not excessively to avoid re-bleeding and dilution of platelets and clotting factors. In conventional resuscitation, small aliquots (15–20 ml/kg) of isotonic crystalloids are administered as a bolus, the patient is reassessed for normalization of cardiovascular parameters in between each bolus and administration is repeated if necessary. Another strategy is 'low volume' resuscitation, where hypertonic crystalloids such as 7.5% saline (2–4 ml/kg), sometimes combined with a colloid (3–5 ml/kg), are administered to normalize cardiovascular status; this has the benefit of minimizing dilution of clotting factors by avoiding the administration of large volumes of isotonic crystalloids. Once the source(s) of haemorrhage has been addressed (e.g. splenectomy), resuscitation may need to be more aggressive to restore appropriate tissue perfusion.

A third strategy usually used only when massive haemorrhage is present or anticipated is 'haemostatic resuscitation'; this involves transfusion of PRBCs and fresh frozen plasma in a 1:1 ratio after initial crystalloid resuscitation, or transfusion of fresh whole blood. The advantage of this approach is that oxygen carrying capacity is provided and dilution of clotting factors and subsequent coagulopathy and re-bleeding is minimized. The disadvantages are the cost and availability of blood products and the risk of transfusion reaction. Due to this, it is usually reserved for patients that appear to have massive haemorrhage or that fail to stabilize by conventional means.

Increasing intra-abdominal pressure using abdominal bandages can be helpful for short-term stabilization to help attenuate intra-abdominal, particularly venous, haemorrhage. Although high intra-abdominal pressures may be reached by these means, it is unlikely that significant arterial haemorrhage will be stopped using an abdominal bandage. Increasing intra-abdominal pressure for prolonged periods of time can have serious consequences to liver, renal and other abdominal organ blood flow; therefore, the long-term (>2–4 hours) use of tight abdominal bandages is not recommended. Surgical therapy is aimed at resection or control of the bleeding focus, removal of any devitalized tissue and biopsy of additional sites of suspicion.

Neoplastic haemoperitoneum

Neoplasia is the most common cause of non-traumatic haemoperitoneum and is common in dogs with splenic malignancy. It has also been reported in association with primary and metastatic hepatic, renal and adrenal malignancies (Aronsohn *et al*., 2009). The majority of splenic malignancies metastasize to the liver and, occasionally, to the lungs. Haemangiosarcoma, in particular, can be identified at multiple sites within the body (spleen, liver, lungs and right atrial appendage). A systematic abdominal ultrasound examination, which can be helpful despite peritoneal fluid, should aid in the diagnosis. Thoracic radiographs should also be made in left and right lateral and ideally dorsal recumbency to assess for gross metastatic disease. Images in sternal recumbency may be taken if the patient's cardiovascular status precludes it being placed on its back safely. If further information about the heart is needed, echocardiography should be performed. Ultrasonographic visualization of the right atrial appendage, however, may be very difficult in the absence of a pericardial effusion. Failure to identify areas of suspicion on radiography or ultrasonography does not rule out pulmonary metastatic disease. With this in mind, surgery is often approached as a procedure to stop further haemorrhage and obtain diagnostic biopsy specimens. However, exploratory laparotomy could uncover findings (e.g. multiple haemorrhaging hepatic masses) that will make proceeding further with surgery an untenable option (Figure 12.15).



12.15 Haemorrhagic splenic mass responsible for haemoperitoneum. Note the multiple masses in the omentum, suggesting local metastatic disease.

Resection of the affected organ or organ part should be carried out as efficiently as possible once the location of the haemorrhage has been identified. In the case of a splenic mass, complete splenectomy is usually the quickest and safest choice even if the disease is limited to just one pole. If the haemorrhagic focus is confined to one or two liver lobes, partial hepatectomy can be considered. Unilateral nephrectomy may be needed if a lesion is present in only one kidney. This procedure is well tolerated in dogs and cats when the remaining kidney has normal function. Although definitive information regarding relative renal function is usually not known for patients undergoing urgent surgery for haemoperitoneum, normal function may be implied if only one kidney contains tumour and the other is grossly normal, and if urine specific gravity, serum creatinine and BUN urea nitrogen were all normal preoperatively. If the haemorrhagic focus is in another abdominal organ, resection should be carried out if it is feasible.

If multiple liver lobes contain bleeding foci, if both kidneys are actively haemorrhaging, or if multiple other sites are bleeding without the presence of a treatable coagulopathy, surgical therapy may be impossible and intraoperative euthanasia is the only reasonable option. If metastatic disease is present throughout the peritoneal cavity, but only one site is actively bleeding, the veterinary surgeon and client have to choose between securing a diagnosis in the hope that medical treatment will be possible, and intraoperative euthanasia. The long-term prognosis for these patients depends upon the tumour type and its biological behavior, with the typical survival for patients with splenic haemangiosarcoma being 10–12 months if adjunctive treatments such as chemotherapy are pursued. Other tumours causing haemoperitoneum such as ruptured hepatocellular carcinoma can lead to survival times of months to years following successful resection.

Postoperative management following surgery for haemoperitoneum

These patients require standard supportive care as for any abdominal surgery, with particular attention paid to development of haemorrhage. This will depend on the underlying disease and the surgery performed; for example, an extensive hepatectomy is much more likely to result in postoperative haemorrhage than a splenectomy. Equally, if extensive metastatic disease was present at other sites, these may begin to bleed at any stage. Serial measurement of PCV and total protein is helpful, and ultrasonography can be used to assess the presence of free peritoneal fluid postoperatively. If haemangiosarcoma is suspected and bleeding occurs, then coagulation testing and appropriate corrective treatment is indicated, as coagulopathy has been reported in dogs with this disease.

Patients receiving large volumes of blood products for resuscitation may develop complications related to electrolyte abnormalities, especially hypocalcaemia caused by citrate anticoagulant, which can be severe and clinically significant. These patients also demonstrate an increased risk of transfusion reactions, which can be mild and self-limiting, such as transient fever, or may be more severe, such as haemolytic reactions or transfusion-related acute lung injury (see Chapter 14). The patient should be closely monitored for development of any of these complications.

Splenic and liver lobe torsion

Splenic and liver lobe torsion are rare conditions associated with haemorrhagic peritoneal effusion. Clinical features of both diseases are inconsistent and non-specific. Splenic torsion is often suspected on the basis of abdominal radiographs and may be further suspected or confirmed by abdominal ultrasonography. Liver lobe torsion may be a difficult diagnosis to make without exploratory laparotomy. Treatment for both conditions is resection. The twisted organ pedicle should not be untwisted prior to resection (see Figure 12.10). There are reports of GDV occurring in dogs with prior splenic torsions, so if the animal is stable, a prophylactic gastropexy may be indicated following removal of the spleen. The prognosis for surgical treatment of these conditions is generally good.

Trauma

Both blunt and penetrating abdominal trauma can result in intra-abdominal haemorrhage. Usually rapid haemorrhage after accidental trauma comes from a laceration or rupture of a major vessel or organ (liver, spleen or kidney). Bleeding from these structures can be rapidly fatal. Other traumatic lesions that cause haemoperitoneum may have less damaging immediate haemodynamic effects but can be equally life-threatening if left undiagnosed. Such conditions include rupture of the urinary bladder, ureteral rupture or avulsion, urethral rupture, gall bladder rupture, and intestinal mesenteric avulsion. Despite all of these possibilities, traumatic haemoperitoneum is often minor, self-limiting and of no long-term significance. Over-exuberant fluid therapy can significantly worsen traumatic haemoperitoneum – see ‘resuscitation strategies in haemo-peritoneum’ above.

Postoperative management and monitoring

Diligent postoperative care and monitoring are essential for successful treatment of abdominal emergency cases. The goals of postoperative management are maintaining adequate tissue perfusion, accompanied by anticipation of and monitoring for potentially life-threatening complications. Although the conditions discussed in this chapter are diverse and cases will vary in severity, these complications may include hypovolaemia due to haemorrhage or fluid losses from the intravascular space, respiratory dysfunction (i.e. aspiration pneumonia), cardiac arrhythmias in dogs with GDV, renal failure, consumptive coagulopathy and sepsis. Frequent clinical, telemetric and laboratory monitoring are vital in critical cases to evaluate cardiac function, perfusion, pulmonary gas exchange, and renal function. The reader is referred elsewhere in this Manual for a more detailed discussion of these methods of monitoring (see Chapters 6, 7 and 8).

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Chapter 13

Haematological emergencies

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Anaemia

Anaemia is defined as a decrease in the red blood cell (RBC) mass secondary to loss (haemorrhage), increased destruction (haemolysis) or decreased production of erythrocytes. The consequences of anaemia are tissue hypoxia, organ dysfunction and, potentially, death. Successful management depends on a systematic diagnostic approach, supportive therapy with blood products, and timely, effective intervention to treat or manage the underlying cause.

Approach in the emergency situation

Anaemic patients are usually presented for progressive weakness, which may culminate in collapse, although occasionally pallor or signs associated with the underlying cause are seen. The duration of clinical signs ranges from peracute to chronic.

All emergency patients should undergo a primary survey to identify abnormalities affecting the major body systems. The patient in an anaemic crisis requires urgent intervention to stabilize life-threatening abnormalities while additional diagnostic evaluation is undertaken (Figure 13.1). Pallor is the hallmark sign of anaemia, but it must be differentiated from pallor associated with hypoperfusion (vasoconstriction) by determination of clinical perfusion parameters and the packed cell volume (PCV).

1. Primary survey.
2. Establish vascular access.
3. Collect pretreatment samples:
   - Minimum database (PCV/TS)
   - Blood smear
   - EDTA blood (for later CBC, reticulocyte count, platelet count, blood typing, immune testing)
   - Serum (for later chemistry profile and/or serological testing)
   - In-saline agglutination test, if haemolysis suspected
   - Citrated plasma, if bleeding suspected (for later coagulation testing).
4. Initiate therapy to stabilize the patient:
   - Support of airway and/or breathing, if indicated
   - Fluid therapy to maintain adequate perfusion
   - Control of haemorrhage, if present
   - Blood transfusion, if indicated.
5. Secondary survey:
   - Complete history
   - Thorough physical examination.
6. Diagnostic work-up (see text).
7. Specific therapy (see text).

13.1 Emergency approach to the anaemic patient. CBC = complete blood count; PCV = packed cell volume; TS = total solids.

Patients in an anaemic crisis are typically obtunded, with marked pallor, tachycardia and bounding (tall, narrow) pulses; they may be tachypnoeic. As such, based on physical examination alone these patients can be difficult to differentiate from those with hypoperfusion due to hypovolaemia, and additional information (determination of PCV) will be required to make this distinction.

Venous access should be achieved by placement of a large-bore peripheral catheter to facilitate aggressive fluid therapy if warranted. Blood should be collected from the catheter for measurement of PCV and total solids (TS); the database may be augmented by measurements of blood glucose, acid–base status, electrolytes, urea and lactate. Wherever possible, samples should be collected prior to initiating therapy to determine baseline results before treatment alters laboratory parameters. Ideally, samples including serum, citrated plasma and EDTA-anticoagulated blood should also be obtained at this time. These samples can be held pending later laboratory submission and for point-of-care tests including blood smear examination, coagulation assessment, blood typing and in-saline agglutination testing.

Patient stabilization should immediately follow blood sample collection. In severe anaemia, blood transfusion is usually required. The decision to transfuse should be based on the patient's clinical signs rather than simply on the PCV. Patients acutely affected even by moderate anaemia may be decompensated, particularly when concurrent hypoperfusion or hypoxaemia exacerbate tissue hypoxia. Conversely, patients with chronic anaemia may tolerate remarkably low PCVs with few clinical signs. Regardless of the rate of onset, however, tissue hypoxia is likely if the PCV is less than 12–15% (Klein *et al*., 2007).

Selection of blood components is based on the PCV and TS. If only the PCV is low, packed red blood cells (PRBCs) should be transfused. If both PCV and TS are decreased, whole blood transfusion is indicated. If only component therapy is available then PRBCs can be administered in combination with crystalloids, plasma or more rarely synthetic colloids. Administration of plasma typically does not provide sufficient albumin to effectively support colloid osmotic pressure, unless very large volumes are given. If a coagulopathy exists, however, a plasma product should be transfused together with PRBCs.

Two intravenous catheters will be required for the concurrent administration of more than one blood product.

First transfusions in dogs need not be type-specific; however, EDTA-anticoagulated samples of the recipient blood should be collected prior to transfusion, and the

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donor should ideally be DEA 1.1 negative. In contrast, all cats must be blood typed and/or crossmatched prior to transfusion to avoid potentially fatal transfusion reactions (Figure 13.2). More information can be found in Chapter 14.

As a rule of thumb, 2 ml/kg of whole blood or 1 ml/kg of PRBCs will increase the recipient's PCV by approximately 1%, dependent on ongoing losses and concurrent fluid therapy. A recent study suggested that an accurate estimate of post-transfusion PCV in dogs could be obtained as follows (Short *et al*., 2012):

$$\text{PCV change (\%)} = \frac{\text{volume administered}}{(\text{bodyweight (kg)} \times 1.5)}$$



13.2 Blood typing must be performed before any feline red cell transfusion. Fatal haemolytic reactions can occur, particularly in blood group B cats administered type A blood. Feline blood typing can be achieved at the point of care using card assays, gel-based systems or immunochromatographic cartridges such as the one shown (DME VET A+B, Alvedia; see Chapter 14).

The aim of transfusion therapy should not be to normalize the patient's PCV, but rather to increase it sufficiently to ameliorate clinical signs. A reasonable target is a PCV of 25–30%.

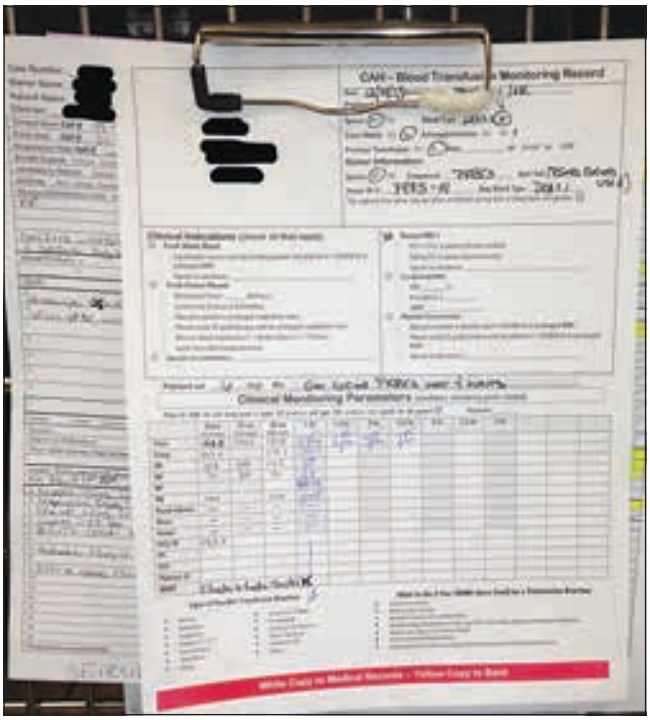
In euvolaemic patients, the recommended transfusion rate is 5 ml/kg/h for dogs and 3 ml/kg/h for cats. In the hypovolaemic patient, this rate can be substantially increased based on individual needs (10–20 ml/kg/h or faster, if necessary). Slower transfusion rates (1–2 ml/kg/h) are recommended in patients with concurrent cardiac disease, hypertension or hyperviscosity disorders. Blood transfusion without concurrent fluid therapy is generally sufficient for the initial stabilization of the euvolaemic anaemic patient, whereas if ongoing haemorrhage is present, blood products are generally combined with other fluid therapy.

All patients should be closely monitored for transfusion reactions during and following resuscitation (Figure 13.3) and the effect of transfusion on PCV and perfusion parameters should be assessed.

Following initiation of stabilization, the secondary survey should be performed. This includes a complete history and thorough physical examination. At this stage, differential diagnoses are determined, and a prioritized and focused diagnostic plan is formulated to determine the cause of the anaemia.

History and physical examination

The signalment of the patient may be informative. Young animals are more likely to have congenital disease or blood loss due to parasites, whereas older animals are at greater risk of malignancies. The history should include detailed enquiries about medications, diet, travel and past illnesses. Current drug therapy may predispose to immune-mediated disease or be associated with marrow suppression or thrombopathia. Dietary indiscretion (e.g. onions, zinc) may result in haemolysis, while travel to certain locations should alert the clinician to the possibility of tick-borne disease or red cell parasites.



13.3 All patients receiving a transfusion should be closely monitored and the data recorded using dedicated forms, to improve identification of a transfusion reaction.

Previous bleeding episodes or the possibility of anticoagulant rodenticide exposure increase the suspicion that haemorrhage is the likely cause of the current anaemia, and the owner should be questioned regarding the presence of signs such as melaena, haematuria or epistaxis. Since many anaemic cats have viral disease, detailed questions should be asked regarding vaccine status and exposure to other cats. The onset of clinical signs is often subtle and not obvious to the owner, but determination via careful questioning may enable the clinician to determine chronicity.

Physical examination should include a thorough search for any evidence of haemorrhage: evaluation of body cavities, examination of the skin, mucous membranes and joints, as well as a rectal examination. The presence of icterus or splenomegaly is an important finding and should raise concern for the possibility of a haemolytic aetiology, though neither is pathognomonic. Fever may result from inflammation, infectious disease, neoplasia or acute immune-mediated haemolysis. The clinician should also actively seek evidence of neoplasia, infectious disease or immune-mediated disease (arthritis, uveitis, glomerulonephritis or cutaneous lesions).

Laboratory assessment

Anaemia is rapidly assessed via PCV measurement. Confirmation of anaemia should be followed by blood smear examination, complete blood count (CBC) and reticulocyte count. In-saline agglutination and direct antiglobulin tests are indicated if haemolysis is suspected. Coagulation testing is indicated if haemorrhage is deemed likely and an obvious cause of haemorrhage is not apparent.

Packed cell volume and total solids

A decreased PCV confirms anaemia. In most cases, PCV approximates haematocrit (Hct); however, the PCV may be significantly higher than the Hct in patients with

macrocytosis, marked reticulocytosis or non-deformable red cells (e.g. spherocytosis). Typically, a concurrent decrease in TS suggests blood loss, whereas normal TS suggests haemolysis or decreased red cell production as the cause. However, the clinician should be aware that refractometric TS measurements can be falsely increased by hyperglycaemia and lipaemia, and are typically decreased by synthetic colloid administration. In dogs with acute blood loss (e.g. following trauma), the PCV may initially be normal or increased due to splenic contraction. Thus, in dogs that have sustained trauma, decreased TS values are an important early clue to active haemorrhage. Splenic contraction does not occur in cats. The plasma should be examined for evidence of haemolysis or icterus (Figure 13.4).

Blood smear examination

Blood smear examination using a Romanowsky type stain (e.g. Diff-Quik®) is likely to be the single most useful tool for evaluating anaemia in the emergency setting. It permits evaluation of the regenerative response (in dogs) and may indicate the cause of the anaemia (Figure 13.5). Increased numbers of reticulocytes are indicative of regeneration. Reticulocytes are seen as larger, more basophilic erythrocytes, resulting in anisocytosis and polychromasia (Figure 13.6). Nucleated RBCs are a less reliable indicator of erythroid hyperplasia, as they may be present in spite of a quiescent marrow (e.g. with neoplasia, lead toxicity, splenic disease, heat stroke). Regeneration cannot be accurately assessed on blood smear examination in cats. Due to the different forms of reticulocytes in cats (see below), the absence of identifiable reticulocytes in this species does not exclude regeneration. Conversely, evidence of any degree of reticulocytosis on blood smear examination in a cat probably indicates an acute and profound regenerative response.

In some cases, erythrocyte morphology may confirm or suggest aetiology. Microcytosis in the non-regenerative anaemic patient suggests iron deficiency or myelophthisis (Figure 13.7). If haemolysis is suspected, erythrocytes should be evaluated for evidence of oxidative damage (Heinz bodies (HB), eccentrocytes), immune-mediated destruction (spherocytes), physical damage (schistocytes) or parasitaemia.

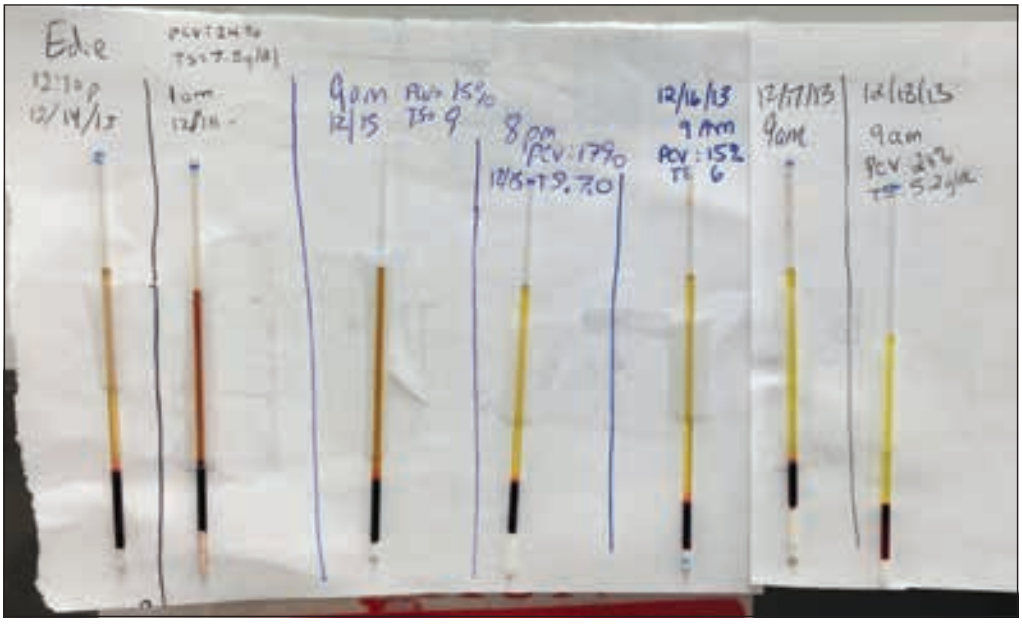
If the patient is bleeding, smear examination is essential to rapidly assess platelet numbers and morphology (see Bleeding disorders below). In addition, leucocyte evaluation enables assessment of white cell numbers and proportions, and may indicate the presence of a left shift, morphological or neoplastic changes, or parasites.

Complete blood count

The CBC determines absolute cell numbers and red cell parameters. Depending on the technology, cell types are typically distinguished based on size (impedance), granularity, and/or light-scattering properties (Moritz and Becker, 2010). In cats, there is often considerable overlap between erythrocyte and platelet volumes, and impedance-based automated cell counters cannot resolve the cells into two distinct populations, resulting in inaccurate counts. Blood smear evaluation is recommended for verification of CBC results in both dogs and cats, particularly when in-house laboratory analysers are used.

Reticulocyte count

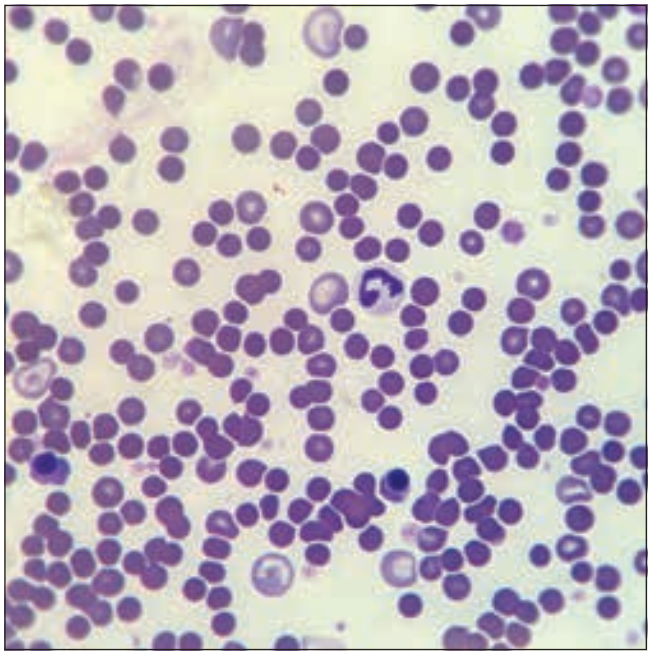
A reticulocyte count should be performed in all anaemic patients to accurately quantify the regenerative response. Reticulocyte counts are performed using supravital staining that enables visualization of ribosomes. A few drops of blood are mixed with an equal volume of 0.5% new methylene blue in physiological saline; 1000 RBCs are counted and the percentage of reticulocytes is recorded. Counting of reticulocytes is uncomplicated in the dog, as the species produces only one reticulocyte type. The cat, however, has two types of reticulocytes: aggregate reticulocytes, in which the organelles are coalesced into aggregates; and punctate reticulocytes, in which the organelles are present as small particles (Figure 13.8). Aggregate forms are released from the marrow and, after approximately 12 hours, develop into punctate forms that persist in the circulation for 10–12 days. Aggregate forms therefore indicate active regeneration, whereas punctate forms indicate recent, cumulative regeneration. Since punctate forms are not recognizable on routine staining, the degree of regeneration may be underestimated in cats. If both forms are counted and not distinguished, active regeneration may



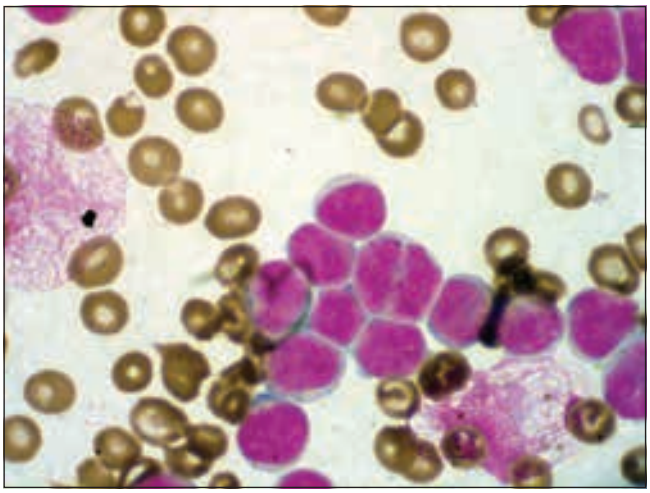
13.4 The plasma component of the blood in microhaematocrit tubes should be scrutinized for haemoglobinaemia or hyperbilirubinaemia. Serial monitoring of these tubes provides a quick visual readout of a patient's progress, here used to monitor a dog with immune-mediated haemolytic anaemia receiving immunosuppressive drugs.

Abnormality	Interpretation
Polychromasia	• Regeneration
Macrocytosis	• Regeneration • Dyserythropoiesis • Feline leukaemia virus infection • Breed-associated (Poodles)
Microcytosis	• Iron deficiency • Copper deficiency • Portosystemic shunt • Breed-associated (Akitas)
Hypochromasia	• Iron deficiency • Copper deficiency
Nucleated red blood cells	• Regeneration • Lead toxicity • Splenic disease • Haemangiosarcoma • Corticosteroid therapy • Systemic stress (cats)
Spherocytosis	• Immune-mediated haemolytic anaemia • Other haemolytic anaemias
Schistocytosis	• Microangiopathy • Haemangiosarcoma • Disseminated intravascular coagulation • Dirofilariasis • Myelofibrosis • Glomerulonephritis
Heinz bodies	• Oxidative red cell injury • May be normal in cats
Eccentrocytosis	• *Allium* spp. toxicity
Codocytosis	• Iron deficiency • Hepatic disease • Post-splenectomy
Parasitic inclusions	• Babesiosis • *Mycoplasma haemofelis* • Distemper inclusion bodies

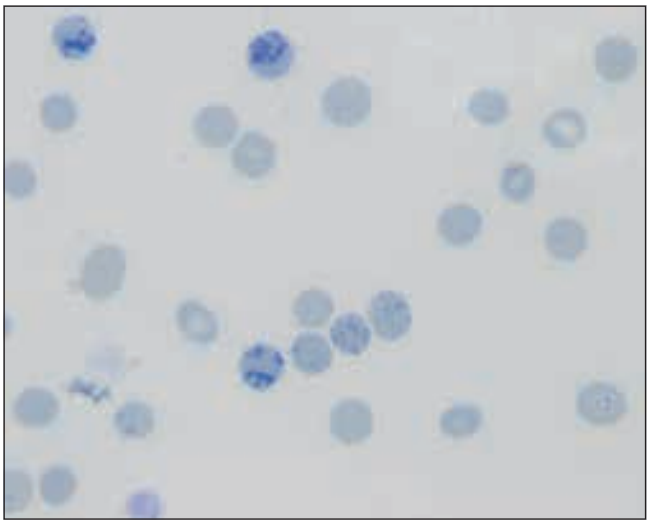
13.5 Common erythrocyte abnormalities observed on blood smear examination.



13.6 Diff-Quik® stained blood smear of a dog with immune-mediated haemolytic anaemia, demonstrating marked polychromasia, anisocytosis, spherocytosis and the presence of nucleated red blood cells (normoblasts).



13.7 Non-regenerative anaemia due to myelophthisis in a patient with lymphoblastic leukaemia.



13.8 Punctate and aggregate reticulocytes in a cat with regenerative anaemia.
(Courtesy of T Stokol, Cornell University)

be overestimated. The degree of reticulocytosis must be interpreted relative to the degree of anaemia, ideally by calculation of the absolute reticulocyte count (number of reticulocytes per litre of blood), where:

Absolute reticulocyte count = observed reticulocyte percentage x RBC number (x 10^9/l)

In dogs, an absolute reticulocyte count exceeding 60 x 10^9/l (60,000/μl) is evidence of regeneration. In cats, aggregate reticulocyte counts greater than 50 x 10^9/l (50,000/μl) are considered regenerative. Alternatively, if the RBC number is not available, a corrected reticulocyte percentage can be calculated as follows:

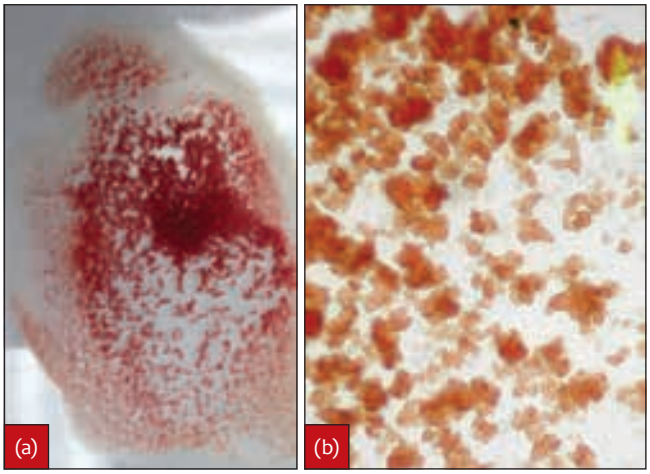
Corrected reticulocyte percentage =
observed reticulocyte count x (PCV/45) (canine)

Corrected reticulocyte percentage =
observed reticulocyte count x (PCV/37) (feline)

A corrected reticulocyte percentage over 1% indicates regeneration.

Saline agglutination test

Screening evaluation for autoagglutination is performed by mixing a drop of blood (fresh or anticoagulated with EDTA) with an equal or greater volume of physiological saline on a glass slide. Autoagglutination, if present, should persist following addition of saline. Macroagglutination can be grossly visualized. Microscopic evaluation of a fresh wet mount will allow detection of microagglutination and differentiation from rouleaux formation (Figure 13.9). If the slide agglutination test is positive, the RBCs should be washed three times. Washing is achieved by centrifugation of an EDTA tube sample, decanting the supernatant and resuspension of the cells in 0.9% saline. Persistent autoagglutination is diagnostic for immune-mediated haemolytic anaemia (IMHA), but is not present in all cases and does not differentiate primary from secondary IMHA.



13.9 (a) Macroagglutination and (b) microagglutination (original magnification X400) from a dog with immune-mediated haemolytic anaemia.

Coagulation testing

Details of coagulation testing are provided in the section on Bleeding disorders later in this chapter.

Diagnostic approach

The essential first step in the diagnostic approach to the anaemic patient is to determine the mechanism of the anaemia: decreased erythropoiesis, haemolysis or haemorrhage (Figure 13.10). Having determined the mechanism of the anaemia, a comprehensive list of differential diagnoses can be constructed and prioritized such that efficient targeted diagnostic testing can be initiated to determine the specific cause.

Regenerative *versus* non-regenerative anaemia

The most important question is to determine whether the anaemia is regenerative or non-regenerative by performing a reticulocyte count or, in the emergency setting, examination of a blood smear (see above). In general, the presence of regeneration indicates that either haemolysis or haemorrhage is the cause of the anaemia, whereas the absence of regeneration suggests that the cause is decreased erythropoiesis. There are, however, three important exceptions:

- Acute haemorrhage or haemolysis of <2–4 days' duration (insufficient time for a marrow response)
- Concomitant disease that precludes an appropriate bone marrow response (e.g. renal failure)
- IMHA in which the immune response targets red cell precursors.

If the anaemia is regenerative, the next step is to determine if it is due to haemolysis or to haemorrhage. If the anaemia is non-regenerative, decreased erythropoiesis is likely but should not be assumed.

Haemolysis

- Antibody-mediated:
  - Immune-mediated haemolytic anaemia
  - Neonatal isoerythrolysis
  - Transfusion reaction
- Toxic:
  - Zinc toxicity
  - Oxidative injury (onions, paracetamol (acetaminophen), propylthiouracil, methylene blue, DL-methionine, lead, cephalosporins, fenbendazole, dapsone, phenacetin, modified live-virus vaccine)
  - Copper toxicosis
- Infectious:
  - Erythroparasites
    - Babesiosis (*Babesia canis*, *B. gibsoni*)
    - Haemobartonellosis (*Haemobartonella canis*, *Mycoplasma haemofelis*)
    - Cytauxoonosis (*Cytauxoon felis*)
    - Ehrlichiosis (*Ehrlichia canis*)
  - Viral
    - Feline leukaemia virus
    - Feline immunodeficiency virus
- Microangiopathic:
  - Disseminated intravascular coagulation
  - Splenic torsion
  - Haemangiosarcoma
  - Vena caval syndrome
- Congenital:
  - Pyruvate kinase deficiency (Basenji, Beagle, West Highland White Terrier, Abyssinian cats)
  - Phosphofructokinase deficiency (English Springer Spaniel, American Cocker Spaniel)
  - Congenital porphyria
  - NADH methaemoglobin reductase deficiency
  - Vitamin B12 deficiency (Giant Schnauzer)
- Miscellaneous:
  - Hypophosphataemia
  - Snake bites

Haemorrhage

- Trauma/surgery
- Bleeding disorders
- Ectoparasites
- Gastrointestinal (endoparasites, ulceration, neoplasia)
- Neoplasia (haemangiosarcoma, others)

Decreased erythropoiesis

- Extra-marrow disease:
  - Anaemia of chronic disease/inflammation
  - Renal failure
  - Endocrine disease (hypoadrenocorticism, hypothyroidism)
  - Feline leukaemia virus
- Intra-marrow disease:
  - Myeloaplasia
  - Drug-associated (chemotherapy, oestrogen, phenylbutazone, griseofulvin, trimethoprim/sulfadiazine, thiacetarsamide, quinidine, chloramphenicol)
  - Infectious (feline leukaemia virus, canine ehrlichiosis, parvovirus)
  - Idiopathic aplastic anaemia
  - Haematopoietic malignancy
  - Myelodysplasia
  - Myelofibrosis
- Nutritional:
  - Iron deficiency
  - Inadequate protein intake

13.10 Causes of anaemia classified by mechanism.

Haemolysis *versus* haemorrhage

Several clinical clues can help to differentiate haemolysis from haemorrhage (Figure 13.11). Blood loss is not always obvious, so a careful search must be made for evidence of bleeding. Physical examination can be augmented by thoracic and abdominal FAST (focused assessment with sonography for trauma) scans to assess for cavity effusions (Boysen and Lisciandro, 2013). In some patients, haemorrhage and haemolysis occur simultaneously. The serum protein concentration is generally normal with haemolysis, and decreased with haemorrhage; there are, however, exceptions – patients with concomitant haemolysis and protein loss (e.g. protein-losing nephropathy) or those with pre-existing hyperglobulinaemia. Haemoglobinaemia and haemoglobinuria indicate haemolysis. Splenomegaly and icterus usually suggest haemolysis, but are neither consistent nor specific findings.

Clinical feature	Haemorrhage	Haemolysis
Evidence of bleeding	Common	Rare
Serum protein (or total solids)	Low (normal)	Normal (high)[a]
Haemoglobinaemia/uria	No	Common
Icterus	No[a]	Common
Splenomegaly	No[a]	Common

13.11 Differentiating haemolysis from haemorrhage. [a]Exceptions can occur in the presence of concurrent or associated disease.

Haemorrhagic anaemia

Significant blood loss can occur externally, or internally into the pleural cavity, the peritoneal cavity, the retroperitoneal space or the fasciomuscular planes. Large volumes of blood can also accumulate in the gastrointestinal tract before melaena becomes evident. When haemorrhage is identified, it is important to determine whether the bleeding is due to local factors or a systemic bleeding disorder (see Bleeding disorders, below). Patients with low-grade chronic blood loss are generally not presented as emergencies until they are severely anaemic due to depletion of iron stores. Since younger animals have smaller stores, they become anaemic more readily than adults, frequently from endo- or ectoparasitism. The anaemia is variably regenerative and is usually microcytic and hypochromic; thrombocytosis may be present. Chronic blood loss in the adult is usually into the gastrointestinal tract. Even when parasites are identified in the adult, additional testing is indicated to eliminate the possibility of an additional cause of haemorrhage (e.g. neoplasia, ulceration).

Haemolytic anaemia

Haemolytic anaemia is common in dogs, often occurring acutely. Most haemolysis is extravascular, with erythrocyte destruction occurring in the spleen and liver. Splenomegaly is frequently present. Intravascular haemolysis is less common, but more severe, and results in haemoglobinaemia and haemoglobinuria. With either process, the rate of erythrocyte destruction may exceed the rate of hepatic clearance, resulting in hyperbilirubinaemia and icterus. The absence of hyperbilirubinaemia, however, does not exclude haemolysis. The evaluation of patients with haemolytic anaemia should always include a blood smear examination and an in-saline agglutination test. Morphological abnormalities highly suggestive of a particular aetiology are frequently detectable on smear examination. These include spherocytes, HBs, eccentrocytes, erythroparasites and schistocytes (see above).

There are numerous causes of haemolytic anaemia, which can be divided into the following major categories:

- Immune-mediated
- Toxic
- Infectious
- Microangiopathic
- Congenital
- Miscellaneous.

A brief description of the most common follows.

Immune-mediated haemolytic anaemia

IMHA is the most common cause of haemolysis in dogs. Haemolysis is usually extravascular, but may be intravascular. IMHA can be primary (idiopathic) or secondary to drug administration (e.g. sulphonamides), neoplasia (especially lymphoma or haemangiosarcoma), tick-borne disease (babesiosis, ehrlichiosis), dirofilariasis or bacterial infection. It is sometimes accompanied by other immune-mediated processes such as immune-mediated thrombocytopenia or systemic lupus erythematosus (SLE). The onset of signs is usually acute. Splenomegaly is common, as are vomiting, icterus and fever. The anaemia is usually regenerative, and neutrophilia is frequent. Thrombocytopenia may also occur, due to antibody-mediated destruction or consumption (thrombosis or disseminated intravascular coagulation (DIC)).

Diagnosis of IMHA requires elimination of other causes of haemolysis and demonstration of immune-mediated erythrocyte injury. Spherocytosis is the most consistent feature of IMHA in canine patients (see Figure 13.6). Autoagglutination is diagnostic for IMHA, but is not consistently present. A positive direct Coombs' test supports the diagnosis, but a negative test does not rule out IMHA. When spherocytosis and autoagglutination are not convincing, and Coombs' testing is negative, an osmotic fragility test may help to identify occult spherocytosis or erythrocyte injury (Paes *et al*., 2013), but is not specific for immune-mediated disease.

If anaemia is non-regenerative, recognition of spherocytes is an important clue to the presence of IMHA (although spherocytes also occur in envenomated dogs). Bone marrow examination usually reveals a distinct maturation block at one stage of erythroid development, with an absence or paucity of later stages due to immune-mediated destruction within the marrow; erythrophagocytosis may also be evident. Immune-mediated pure red cell aplasia can also occur, due to destruction of stem cells. Diagnosis of immune-mediated anaemia in these cases can be difficult, and response to therapy provides important information. In cases of non-regenerative IMHA, a longer period should be anticipated for response to therapy (weeks to months).

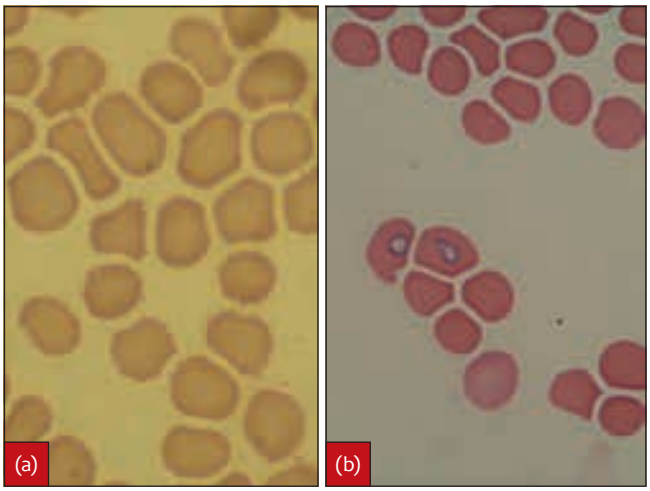
The diagnosis of IMHA should prompt a thorough search for underlying causes or systemic immune-mediated disease. In addition to a CBC, biochemical profile, urinalysis and culture, diagnostic tests should include thoracic radiology, abdominal radiology or ultrasonography, an antinuclear antibody (ANA) test and serology for tick-borne diseases and occult dirofilariasis. Testing for infectious diseases should be based on geographical location and patient travel history. Testing for neoplasia should be performed prior to the initiation of corticosteroid therapy, which can preclude diagnosis.

IMHA is less common in the cat. Because recognition of feline spherocytes is difficult, the osmotic fragility test may be performed as a proxy measure of the degree of spherocytosis. Primary IMHA appears to be infrequent in the cat, so an underlying aetiology should be aggressively sought. Infection with *Mycoplasma haemofelis* is frequently associated with IMHA (Figure 13.12). Cats should also be evaluated for neoplasia and for viral disease.

Treatment of IMHA includes the elimination or management of any underlying cause, adequate immunosuppression and appropriate supportive care. Glucocorticoids are the mainstay of immunosuppressive therapy, and following diagnosis and testing for underlying neoplasia, should be initiated without delay. Various glucocorticoids may be used, with the commonest being prednisolone (1–2 mg/kg q12h orally or s.c. for patients under 10 kg, and 15 mg/m^2 q12h for patients above 10 kg) or dexamethasone (0.2–0.4 mg/kg i.v. q24h). When tick-borne disease is possible, doxycycline should be administered (10 mg/kg orally or slow i.v. q24h) pending confirmatory testing. The guidelines for blood transfusion are as with other forms of anaemia. Blood transfusion with PRBCs is indicated for the IMHA patient with clinical signs referable to the anaemia.

Response to therapy is assessed by the Hct, which reflects the balance between erythrocyte destruction and the bone marrow regenerative response. Most patients with regenerative IMHA respond to glucocorticoid therapy within 5–7 days, as evidenced by stabilization and then increased Hct. Corticosteroids are continued at the initial dosage until the Hct normalizes, usually a minimum of 2–4 weeks. They are then gradually tapered over subsequent months (usually by 25–50% every 3–4 weeks, based on Hct monitoring).

Adjunctive immunosuppressive drugs are often used during the induction phase in patients with intravascular haemolysis, autoagglutination, severe hyperbilirubinaemia or unrelenting aggressive haemolysis, although their efficacy in these scenarios remains to be firmly established. These drugs are also prescribed in an attempt to provide a synergistic immunosuppressive effect, thus allowing for more rapid tapering of the corticosteroid. In addition, they are commonly used in the later phases of treatment if unacceptable corticosteroid adverse effects occur, or if corticosteroid dosage reduction results in relapse.



13.12 Anaemia may be secondary to infectious diseases in both dogs and cats. Here punctate forms of (a) *Mycoplasma haemofelis* can be seen associated with the erythrocyte membrane. (b) The characteristic basophilic piriform shapes of *Babesia canis* can be clearly seen in the erythrocytes of this dog with a history of travel to Spain.

Several adjunctive immunosuppressive drugs may be considered, but the optimal strategy remains unclear. In the dog, azathioprine is commonly prescribed (2.2 mg/kg q24h in small and medium-sized dogs, and 1.5 mg/kg q24h in larger dogs), although its efficacy has been questioned (Piek *et al*., 2011b). Potential adverse effects include myelosuppression and hepatopathy. Regular monitoring of CBC (every 2–4 weeks) is recommended, particularly if daily dosing is continued for a prolonged period. Intermittent monitoring of hepatic parameters is also prudent. Azathioprine should not be used in cats. Ciclosporin (3–7 mg/kg orally q12h in dogs; 4–6 mg/kg orally q12h in cats) is an attractive option for adjunct immunosuppression as it is not myelosuppressive. Moreover, because of its rapid onset of action, it is an option in the acute scenario. Mycophenolate mofetil (10–15 mg/kg orally or i.v. q12h in the dog) has been suggested to have equivalent efficacy to other adjunctive immunosuppressives, although gastrointestinal side effects can be limiting (Wang *et al*., 2013; West and Hart, 2013). Cyclophosphamide should be avoided due to the potential for myelosuppression. Although the use of human intravenous immunoglobulin (hIVIG) has been described for IMHA in dogs, efficacy is uncertain. This, considered together with the risk of anaphylaxis and the associated expense, mean it is difficult to justify its use for this purpose at this time (Whelan *et al*., 2009).

IMHA is associated with a hypercoagulable state and thromboembolism, particularly pulmonary thromboembolism (PTE) (Sinnott and Otto 2009; Goggs *et al*., 2012). The pathophysiology is complex and includes increased intravascular tissue factor (TF) expression secondary to the marked inflammatory response that accompanies the disease as well as increased platelet activation (Piek *et al*., 2011a; Kidd and Mackman, 2013). Thromboembolic risk is exacerbated by stasis, immobility, vascular catheterization and corticosteroid therapy.

While the use of antithrombotics is recommended, there is much controversy surrounding the ideal drug and protocol (Goggs *et al*., 2009). A 2005 study suggested that ultralow-dose aspirin (0.5 mg/kg q24h) may improve survival in dogs with IMHA (Weinkle *et al*., 2005), but concerns about treatment bias and a lack of replication have limited acceptance (Orcutt *et al*., 2009). The use of clopidogrel for thromboprophylaxis has also been investigated (Mellett *et al*., 2011), but a benefit over aspirin is yet to be demonstrated in dogs. Limited evidence suggests that the use of unfractionated heparin may be more efficacious, but close monitoring and individual dose adjustment is essential to maximise the benefit/risk profile of this intervention (Breuhl *et al*., 2009; Helmond *et al*., 2010). Recently, use of rivaroxaban, an oral direct anticoagulant, has been reported for IMHA, and this drug type may represent an ideal combination of efficacy, safety and ease of use in the future (Morassi *et al*., 2016). At this time, however, the most appropriate and effective drug or dosing regimen for thromboprophylaxis in patients with IMHA remains unclear.

The prognosis for animals with IMHA is variable. Recent reports suggest a mortality rate of approximately 30%, with improved overall prognosis for patients that survive the initially high-mortality in-hospital period (Piek *et al*., 2008). A poorer prognosis is associated with intravascular haemolysis, severe hyperbilirubinaemia and neoplasia. Thromboembolic complications, particularly PTE, are common and significantly worsen the prognosis. A small proportion of cases may have protracted disease that precludes discontinuation of corticosteroids. Relapse is possible.

Zinc toxicity

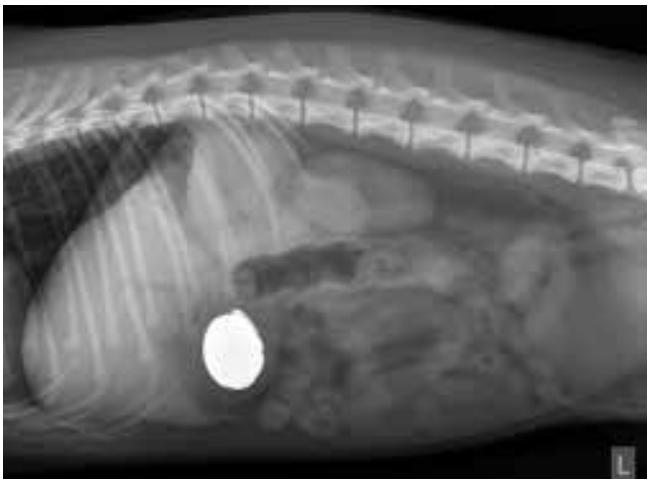
The ingestion of certain coins (e.g. UK £1 and £2 coins, higher denomination Euros and US pennies), zinc nuts, bolts or screws, or topical skin protectants can result in toxic concentrations of zinc, causing severe intravascular haemolysis, gastrointestinal irritation and, in some cases, pancreatitis. Haemolysis is intravascular, resulting in haemoglobinaemia and haemoglobinuria (Figure 13.13). Zinc toxicity should be suspected in any patient with acute haemolytic anaemia in the absence of autoagglutination or significant erythrocyte morphological abnormalities (although occasional spherocytes may be noted in zinc intoxication). A tentative diagnosis is based on a history of exposure, and radiographic evidence of metallic foreign objects in the gastrointestinal tract (Figure 13.14). Since the mere presence of metallic foreign bodies does not confirm zinc toxicity, and zinc toxicity can occur in the absence of metal ingestion, definitive diagnosis requires the presence of convincing clinical signs and an elevated blood zinc concentration. Due to the high mortality associated with zinc toxicity, these patients constitute serious emergencies and treatment should not be delayed pending the results of zinc concentrations.

Treatment of zinc toxicity begins with patient stabilization, followed by prompt removal of the suspect object(s), when present, via endoscopy or laparotomy; this usually leads to a rapid fall in blood zinc levels. Appropriate fluid therapy is based on perfusion parameters and renal function, and PRBCs should be transfused as necessary. Antacids, such as omeprazole (1 mg/kg orally or slow i.v. q24h) are recommended to decrease gastric acidity and 'leaching' of zinc from the source. Chelation therapy is controversial and rarely necessary if the source of zinc can be removed. If removal is not possible, and chelation is required, calcium disodium EDTA is typically recommended (25 mg/kg i.v. q6h). Where feasible, the decision to use chelators should be based on serum zinc concentrations. The prognosis for complete recovery is excellent with timely and aggressive intervention.





13.13 (a) Profound haemoglobinuria due to zinc intoxication secondary to ingestion of (b) a large number of zinc-containing coins. UK £1 and £2 coins, higher denomination Euros and US pennies are common sources of zinc. Immune-mediated haemolytic anaemia is the major differential diagnosis for the haemolysis of zinc intoxication, and differentiating the two can be challenging because spherocytosis can also occur in zinc intoxication.

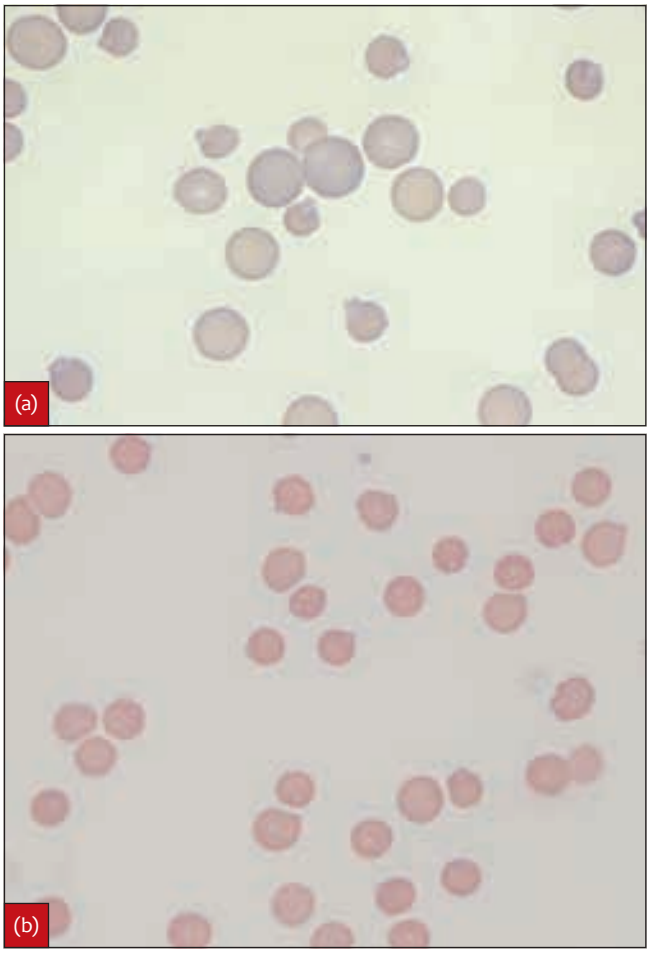


13.14 In contrast to immune-mediated haemolytic anaemia patients, dogs with zinc intoxication typically have evidence of metallic foreign bodies. Abdominal radiography confirms the presence of the foreign objects, although zinc-containing skin creams may be more difficult to identify radiographically. The dog in this radiograph developed marked haemolysis necessitating transfusion of packed red blood cells. Endoscopic removal of the objects (zinc washers) led to a rapid resolution of clinical signs.

Oxidative injury

Oxidative injury leads to denaturation of haemoglobin, resulting in HB formation, or oxidation of ferrous iron (Fe^{2+}) to the ferric form (Fe^{3+}), resulting in methaemoglobinaemia. HBs cause decreased erythrocyte deformability and survival. The most common cause of HBs in the dog is the ingestion of onions or other *Allium* species such as garlic or chives (raw, cooked or dried). HBs usually appear within 24 hours of exposure, with haemolysis occurring approximately 5 days post-ingestion. HBs are best identified on blood smear examination using new methylene blue staining. In the dog, HBs are usually small, occur in multiples and, when large, may be seen as clear 'blebs' protruding from the cell surface. Eccentrocytes, erythrocytes in which the haemoglobin is displaced to one side, frequently accompany HBs in this species.

Feline haemoglobin is highly sensitive to oxidative denaturation, and HB formation is common in the cat, such that low numbers can be present under normal physiological conditions. HBs can also accompany numerous diseases in cats, including lymphoma, hyperthyroidism and diabetes mellitus. A variety of substances, including pharmaceuticals such as propofol, may induce HB formation and severe anaemia in cats (Andress *et al*., 1995). Commercial cat foods and drug preparations containing propylene glycol are associated with susceptibility to oxidative injury and HB formation, but do not generally result in clinical anaemia. The diagnosis of overt HB anaemia requires visualization of relatively large HBs in many erythrocytes, together with convincing evidence of haemolysis. In the cat, HBs are typically single (Figure 13.15). The management of HB anaemia includes removal of the causative agent or treatment of the underlying disease and supportive care, including blood transfusion where indicated.



13.15 Heinz bodies in (a) a cat and (b) a dog, following onion ingestion. Both were stained using modified Wright's stain.
(Courtesy of T Stokol, Cornell University)

Erythroparasites

Mycoplasma haemofelis (previously *Haemobartonella felis*) can cause acute anaemia, especially in cats with underlying immunosuppressive disease, such as feline leukaemia virus (FeLV) or feline immunodeficiency virus (FIV). Diagnosis relies on visualization of the organism on erythrocytes via blood smear examination (see Figure 13.12), or on confirmation of the presence of parasite DNA via polymerase chain reaction (PCR). Due to waxing and waning parasitaemia, parasite visualization may require smear examination on several consecutive days. The organism may appear as ring, punctate or rod forms. Ring forms consist of a fine basophilic ring with a clear centre. Punctate and rod forms are observed on the periphery of the cell. Because the organisms are epicellular, they can be easily dislodged from the cells in EDTA. Identification is thus best achieved by examination of a fresh blood smear. Prolonged alcohol fixation during staining can also displace organisms. The disease is treated with tetracycline (20 mg/kg orally q8h) or doxycycline (5 mg/kg orally q12h) for 2–3 weeks. Concurrent corticosteroid therapy has been advocated, since an immune-mediated process is likely. Specific and supportive therapy for concurrent disease should be provided as appropriate.

Haemobartonella canis is rare, usually occurring only in splenectomized, severely debilitated or immunosuppressed dogs. Organisms are readily identified on smear examination, as chains on the surface of erythrocytes. Spherocytosis is common, suggesting an immune-mediated pathophysiology. Treatment is with tetracyclines, using the same regimen as for the cat. Immunosuppressive corticosteroid therapy should be considered if response to antibiotics alone is inadequate.

The tick-transmitted protozoans, *Babesia canis* and *Babesia gibsoni* cause haemolytic anaemia in dogs. Clinical manifestations range from acute disease with severe intravascular haemolysis to subacute or chronic disease with mild or moderate anaemia. Immune-mediated haemolysis appears to occur frequently and, dependent on geographical location, concurrent infection with *Ehrlichia canis* is not uncommon. Complicated cases of babesiosis may manifest as DIC, respiratory distress or the systemic inflammatory response syndrome (Jacobson, 2006). Diagnosis of babesiosis can be achieved by identification of intra-erythrocytic pyriform bodies on blood smear examination (see Figure 13.12). Since parasitized erythrocytes tend to 'sludge' in the capillaries, diagnostic yield is improved by evaluation of an earstick blood smear. Serological or PCR testing is indicated when infection is suspected but, organisms cannot be found. Diagnostic work-up should also include evaluation for IMHA and serological testing for ehrlichiosis. Treatment includes appropriate supportive therapy and specific antiparasitic drugs, such as diminazine aceturate, imidocarb dipropionate or atovaquone/azithromycin (Birkenheuer, 2012).

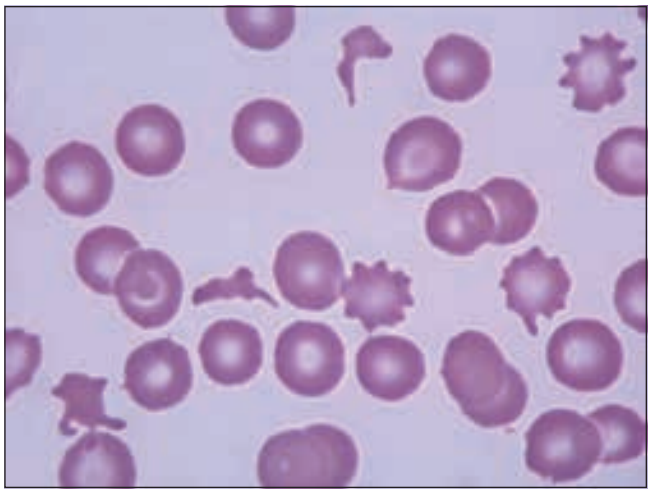
Congenital disorders

Inherited enzyme deficiencies are rare and, because signs can mimic IMHA, diagnosis may be missed. Phosphofructokinase (PFK) deficiency has been described in English Springer and American Cocker Spaniels. Chronic mild to moderate anaemia occurs, with superimposed episodes of intravascular haemolysis precipitated by vigorous exercise or panting, due to the sensitivity of PFK-deficient erythrocytes to alkalaemia. Affected dogs are typically presented at a young age with acute intravascular haemolysis and a strong regenerative response that recovers spontaneously. If immunosuppressive therapy is initiated, recovery may be erroneously ascribed to the drug. The diagnosis of PFK deficiency is confirmed by enzyme assay performed by specialized laboratories (Harvey, 2006).

Pyruvate kinase (PK) deficiency has been described in Basenjis and Beagles. It is characterized by chronic severe haemolysis and moderate to severe anaemia, usually first recognized at 3–6 months of age. The Hct slowly declines over the subsequent 1–3 years. Typically, the anaemia is initially highly regenerative, but terminal myelofibrosis may develop. Definitive diagnosis of PK deficiency is via enzyme assay performed by specialized laboratories, but the availability of such testing is limited. The identification of the underlying mutations has enabled the development of breed-specific PCR-based genetic testing, which is now widely available (http://www.thekennelclub.org.uk/media/14688/dnatestsworldwide.pdf).

Microangiopathy

Microangiopathic haemolytic anaemia results from mechanical fragmentation of erythrocytes. Causes include splenic torsion, haemangiosarcoma, DIC and caval syndrome associated with heartworm disease. Erythrocyte fragmentation is recognized by the presence of schistocytes (sheared erythrocytes) on blood smear examination (Figure 13.16). Ordinarily, anaemia is subclinical but, in severe cases, overt anaemia develops (e.g. splenic torsion or heartworm-induced caval syndrome).



13.16 The presence of schistocytes (sheared erythrocytes) on blood smear examination should alert the clinician to the possibility of microangiopathic disorders such as disseminated intravascular coagulation or haemangiosarcoma. Schistocytes may also be seen in patients with caval syndrome associated with dirofilariasis.
(Courtesy of T Stokol, Cornell University)

Decreased erythropoiesis

Decreased erythropoiesis can result from extra-marrow or intra-marrow disease. Anaemia caused by an extra-marrow disorder occurs when a systemic disease selectively depresses erythropoiesis. The anaemia that develops is generally mild (Hct range 25–35% in dogs, and 20–25% in cats) and because the anaemia develops slowly, clinical signs of the underlying disease usually predominate. In contrast, intra-marrow diseases, such as aplastic anaemia, myelodysplasia, myeloproliferative disorders and myelofibrosis, result from injury to the stem cells and/or the marrow microenvironment. Depending on the course of the disease, variable cytopenias are observed.

Acute marrow disease is usually characterized by granulocytopenia and thrombocytopenia, with mild to non-existent anaemia. Chronic marrow disease is characterized by moderate to severe anaemia, with variable degrees of leucopenia and thrombocytopenia.

Evaluation of the patient with non-regenerative anaemia should include investigation into possible drug exposure, CBC to determine other blood cell counts, evaluation for systemic disease, serological testing for FeLV and FIV in the cat and for ehrlichiosis in the dog, and bone marrow examination. Bone marrow aspirate may reveal evidence of neoplasia or dysplasia, and allows estimation of cellularity (Weiss, 2005). Non-regenerative IMHA, in which erythrocyte precursors are targeted by the immune system, is often suggested by marrow examination (Weiss, 2008). A core bone marrow biopsy, however, is necessary to determine fully the degree of cellularity or fibrosis, and to accurately assess maturation sequences. Treatment of non-regenerative anaemia depends on the cause, and may include blood transfusion and/or colony stimulating factors (Langston *et al*., 2003; Weiss, 2003).

Bleeding disorders

Bleeding disorders are classified as primary (platelet or vascular disorders) or secondary (coagulation factor disorders) and can be inherited or acquired. Bleeding disorders should always be considered life-threatening since even the stable patient with a bleeding disorder can decompensate rapidly and without pre-emptive signs. Rapid diagnosis and institution of rational therapy are paramount.

Approach in the emergency situation

Animals in haemorrhagic crisis usually show signs of hypovolaemic shock. Blood samples should be collected prior to initiating therapy, and should include a PCV and TS, a blood smear, and EDTA- and citrate-anticoagulated blood and serum for later laboratory testing. PCV and TS are usually decreased in the bleeding patient. In canine acute haemorrhage, the PCV may be normal or elevated due to compensatory splenic contraction, but the TS is usually low, reflecting blood loss. A blood smear should be examined, with emphasis on platelet numbers and morphology and the presence of schistocytes. Depending on the findings in the individual patient, further testing may include a CBC, chemistry profile, coagulation testing, and immune and/or serological testing.

Stabilization of the bleeding patient requires control of haemorrhage and blood volume replacement. The most life-threatening problem is shock, so initial therapy should involve aggressive fluid replacement (crystalloid with or without synthetic colloids) until blood is available. Animals should be kept quiet and unstressed, subcutaneous injections should be avoided and venepuncture performed only when required for platelet enumeration. Following venepuncture, the site should be held off with firm manual pressure for 5 minutes. Jugular sampling should be avoided. A peripheral intravenous catheter can usually be safely placed and used to collect all other blood samples (including regular PCV monitoring). Patients should be closely monitored for evidence of ongoing haemorrhage, including evaluation of perfusion, respiratory rate and effort, mucous membrane colour, neurological status and PCV/TS.

Once the patient has been stabilized, three initial questions must be answered:

- Is the bleeding due to local factors or is a generalized haemostatic abnormality present?
- If a systemic bleeding disorder exists, what is the nature of the haemostatic defect?
- Is the defect congenital or acquired?

These questions can generally be answered based on the history, physical examination and routine coagulation tests.

Pathophysiology

Haemostasis can be divided into two distinct but overlapping phases: primary haemostasis, involving the interaction between platelets and endothelium resulting in the formation of a platelet plug, and secondary haemostasis, a system of proteolytic reactions involving coagulation factors and resulting in the generation of fibrin polymers, which stabilize the platelet plug to form a mature thrombus. These phases occur concomitantly and, under normal physiological conditions, intrinsic regulatory mechanisms contain thrombus formation both temporally and spatially. Fibrinolysis is the dissolution of the fibrin clot to restore vascular patency. The delicate balance between proteolytic and inhibitory reactions in haemostasis and fibrinolysis can be disrupted by inherent or acquired defects, resulting in abnormal bleeding.

Primary haemostasis immediately follows vascular injury. Platelets adhere to the subendothelial collagen,

mediated by von Willebrand factor (VWF) and membrane glycoproteins. Following adherence, the platelets undergo conformational changes and release bioactive substances that stimulate platelet aggregation. Aggregated platelets constitute the primary haemostatic plug and expose phosphatidylserine, which is an essential component of the coagulation factor complexes that assemble on platelet surfaces. Defects in primary haemostasis are due to platelet or vascular disorders. Platelet disorders can be quantitative (thrombocytopenia) or qualitative (thrombopathia). Vasculopathies lead to excessive fragility or abnormal platelet–endothelial interaction.

Secondary haemostasis involves the formation of fibrin by the activation and subsequent formation of coagulation factor complexes on the surfaces of activated platelets. All coagulation factors are produced in the liver, with the exception of factor VIII. Vitamin K is required for the activation of factors II, VII, IX and X, as well as protein C. The traditional model of coagulation consists of a cascade of enzymatic reactions, in which enzymes cleave substrates to generate the next enzyme in the cascade. This model is divided into two pathways: the 'extrinsic' pathway, initiated by TF, and the 'intrinsic' pathway, initiated through contact activation of factor XII. These two pathways converge into a final common pathway of thrombin generation and fibrin formation. Although this model is valid for interpretation of traditional *in vitro* coagulation testing, it does not adequately explain coagulation *in vivo*.

A cell-based model of coagulation more accurately reflects coagulation *in vivo* (Hoffman and Monroe, 2001; Smith, 2009). This model includes two fundamental paradigm shifts: that TF is the primary physiological initiator of coagulation, and that coagulation is localized to, and controlled by, cellular surfaces. In this model, coagulation occurs in three overlapping phases: initiation (on TF-bearing cells), amplification, and propagation (on platelets). The initiation phase is the TF-initiated ('extrinsic') pathway that generates small amounts of thrombin. During the amplification phase, platelets are activated and have activated cofactors V and VIII bound to their surfaces. In this manner, thrombin amplifies the initial signal, acting on the platelet to set the stage for procoagulant complex assembly. During the propagation phase, complexes are assembled on the surface of the activated platelet, and large-scale thrombin generation occurs (similar to the previously named 'intrinsic' pathway). This provides the burst of thrombin necessary to produce large quantities of fibrin. Fibrin monomers are then complexed to form fibrin polymers and a stable thrombus.

Fibrinolysis is the enzymatic dissolution of fibrin. Plasminogen activators proteolytically convert plasminogen to plasmin, which in turn degrades fibrin into soluble fibrin degradation products (FDPs). FDPs have anticoagulant activity by interfering with platelet function and inhibiting thrombin. They are ultimately removed from the circulation by the liver (half-life approximately 9–12 hours). Excessive fibrinolysis and generation of FDPs can occur in conditions such as DIC and hepatic disease, and may contribute to a bleeding tendency. D-dimers represent the breakdown products of cross-linked fibrin and are a more specific measure of fibrinolysis and thrombosis. Few disorders of fibrinolysis have been described in small animals to date, which probably reflects our limited ability to interrogate this component of the haemostatic system. Recent diagnostic developments in this area will improve our understanding of this field in the future (Brooks *et al*., 2011; Brooks and Catalfamo, 2013).

Clinical and laboratory assessment

Following initial stabilization of the bleeding patient, the next step is to determine whether haemorrhage is due to a systemic bleeding disorder or to a local cause. Bleeding disorders should be categorized as defects of primary or secondary haemostasis, or both (Figure 13.17). If the bleeding disorder does not readily fit this classification, then a fibrinolytic disorder should also be considered. The history and physical examination often provide important clues, but definitive classification requires laboratory testing.

Disorders of primary haemostasis
• Petechiae, ecchymoses – common • Haematomas – rare • Mucosal surface bleeding, including gastrointestinal – common • Bleeding into body cavities and joints – rare • Bleeding usually at multiple locations • Prolonged and repeated bleeding from cuts (rebleed)
Disorders of secondary haemostasis
• Petechiae, ecchymoses – rare • Haematomas – common • Mucosal surface bleeding – rare • Bleeding into body cavities and joints – common • Bleeding frequently localized • Bleeding may be delayed in onset

13.17 Clinical features associated with primary and secondary haemostatic disorders.

History

Bleeding is not always evident to the pet owner. Some animals with bleeding disorders are presented for apparently unrelated disease; for example, shifting leg lameness may result from recurrent haemarthrosis, and acute blindness may be due to hyphaema.

A detailed history is essential. Severe inherited disorders are generally apparent within the first 6 months of life; milder forms may not be diagnosed until surgery, trauma or concurrent disease intervene. Certain inherited disorders are breed related, for example, von Willebrand's disease (VWD) in the Dobermann. It is important to ascertain whether previous bleeding episodes have occurred in the patient, or in family members. The patient's response to prior trauma or surgery may allow the clinician to date the onset of the disorder; a patient that has tolerated surgery is unlikely to have a severe inherited bleeding disorder. The history should include detailed enquiries about previous illnesses and medications. Certain drugs (notably sulphonamides and penicillins) may cause thrombocytopenia 3–10 days post-treatment (Weiss, 2012). Specific enquiries about the environment and patient behaviour may reveal the potential for exposure to infectious disease, toxins or trauma.

Physical examination

Evaluation of the distribution, extent and nature of current haemorrhage requires careful examination of all body systems, including the skin, mucous membranes, eyes and joints, as well as the urine and faeces. The nature of the haemorrhage helps to characterize the haemostatic defect. Petechiation, ecchymosis and spontaneous bleeding from mucosal surfaces (including epistaxis, gingival bleeding, haematuria, melaena and ocular haemorrhage) characterize defects of primary haemostasis (Figure 13.18). However, platelet and vascular abnormalities generally cannot be distinguished on physical examination alone. Defects of secondary haemostasis are usually characterized by single



13.18 Physical examination abnormalities consistent with a primary haemostatic disorder. (a) Petechiation. (b) Ecchymoses. (c) Inguinal bruising. (d) Episcleral (subconjunctival) haemorrhage. (e) Mild hyphaema noted as iris haemorrhage. (f) Marked hyphaema with blood in the anterior chamber.

or multiple haematomas and bleeding into subcutaneous tissue, body cavities, muscles or joints. Some acquired abnormalities, such as DIC, defy this classification because multiple haemostatic defects are present. Likewise, VWD usually has the characteristics of a primary haemostatic defect, but in its most severe form may mimic a secondary haemostatic disorder. The physical examination should also aim to identify any evidence of concurrent or underlying disease, such as neoplasia, infectious or immune-mediated disease. This requires examination for masses, organomegaly, lymphadenopathy, uveitis, chorioretinitis, mucocutaneous lesions and arthropathy.

Routine coagulation testing

Laboratory tests are essential to confirm and characterize the haemostatic defect; normal values are presented in Figure 13.19. These tests should be performed and interpreted carefully (Figure 13.20), together with the clinical findings. Blood samples should be collected via atraumatic venepuncture prior to the initiation of therapy. The jugular vein should be avoided where possible in patients with a suspected coagulation disorder because application of sufficient pressure to stop bleeding may be difficult and blood loss following jugular venepuncture can be occult.

Variable	Dog	Cat
Platelet count (x 10^9/l)	200–450	200–600
Buccal mucosal bleeding time (minutes)	1.7–4.2	1.4–2.4
Activated clotting time (seconds)	60–110	50–75
Prothrombin time (seconds, CoagDx)	12–17	12–23
Activated partial thromboplastin time (seconds, CoagDx)	71–102	70–129
D-dimers (ng/ml)	<250	<250
Antithrombin (%)	65–145	75–110
Fibrinogen (mmol/l)	4.4–14.4	2.2–7.9

13.19 Normal values for screening coagulation tests.

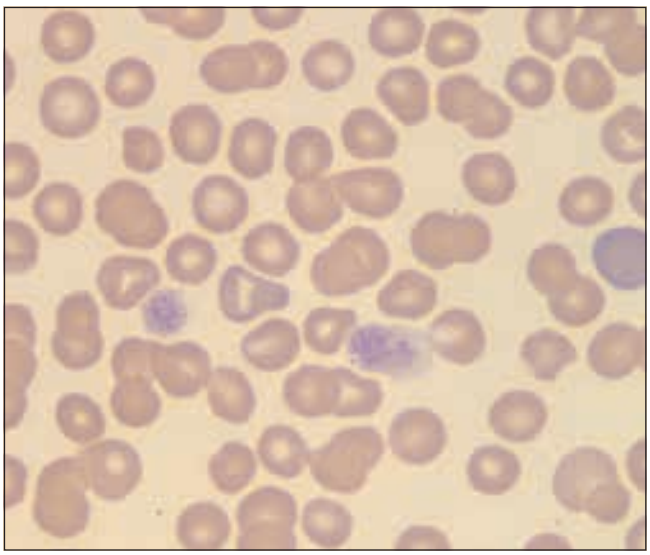
Process	Screening test	Component/factors evaluated
Primary haemostasis	Platelet count	Platelet numbers
	BMBT	Platelet numbers and function Endothelial function
	PFA-100	Platelet function
	Platelet aggregometry	Platelet function
	TEG/ROTEM	Platelet number and function, coagulation factors, haematocrit
Secondary haemostasis	Fibrinogen (Fg)	Fibrinogen concentration
	Prothrombin time (PT)	Factors VII:TF, X, V, II and Fg
	Activated partial thromboplastin time (aPTT)	Factors XII, XI, IX, VIII, X, V, II and Fg
	Activated clotting time (ACT)	Factors XII, XI, IX, VIII, X, V, II and Fg
	Thrombin time (TT)	Fibrinogen concentration and quality
Fibrinolysis	D-dimers	Lysis of cross-linked fibrin
	TPA TEG/ROTEM	Endogenous fibrinolytic potential

13.20 Screening tests for evaluation of haemostatic disorders. BMBT = buccal mucosal bleeding time; PFA = Platelet Function Analyzer; ROTEM = thromboelastometry; TEG = thromboelastography; TF = tissue factor; TPA = tissue plasminogen activator.

Platelet enumeration/estimation: Quantitative platelet disorders are detected via platelet count. This should be performed in all patients with a suspected bleeding disorder. Samples should be collected into EDTA and analysed within 12 hours of collection, either manually (by haemocytometer) or by an automated cell counter. Both techniques are reliable for canine blood. In cats there is considerable overlap between erythrocyte and platelet volumes, resulting in erroneous results from automated counters. Feline platelets should therefore be enumerated manually.

Examination of a blood smear enables rapid estimation of platelet numbers. This is essential in the emergency setting, where automated counts may not be available, and in cats, where automated counts are frequently inaccurate. Because platelet clumping during sampling is common, and results in artefactual low counts (pseudothrombocytopenia), blood smear examination should always be performed to verify (or refute) a low platelet count. In a well distributed smear, an average of approximately 10–25 platelets per high-power field (hpf) (X1000 magnification) is considered normal. As a general rule, each platelet in such a field represents a count of approximately 15,000/μl. Individuals of some breeds (notably Cavalier King Charles Spaniels and Greyhounds) may normally have a lower number of larger platelets (Figure 13.21). Spontaneous bleeding due to thrombocytopenia alone generally does not occur until platelet counts are below 40,000/μl, or 2–3/hpf. The presence of platelet clumping, best visualized at the feathered edge of the smear, indicates that both the platelet count and the estimate will be artefactually low. However, the existence of platelet clumps means a significant thrombocytopenia is unlikely. The absence of clumping must be confirmed before a diagnosis of thrombocytopenia is made. Large platelets (macroplatelets) generally indicate megakaryocytic hyperplasia and a regenerative response. The blood smear should also be examined for schistocytes, which suggest microangiopathy or DIC, causes of consumptive thrombocytopenia.

Bleeding time: The bleeding time is the duration of haemorrhage resulting from the infliction of a small, standardized injury involving microscopic vessels. The buccal mucosal bleeding time (BMBT) is the most reliable and reproducible method. Cats usually require light sedation. The patient is restrained in lateral recumbency and a strip of gauze can be tied around the maxilla to fold up the upper lip. A two-blade, spring-loaded device is used to make two 1 mm deep incisions in the mucosa of the upper lip (Figure 13.22). The incisions should be made at a site devoid of visible vessels and inclined so that the blood flows towards the mouth. Shed blood is carefully blotted with filter paper, taking care not to disturb the incision sites. The time from incision to cessation of bleeding is measured. The bleeding time reflects *in vivo* primary haemostasis. It may be prolonged by thrombocytopenia, thrombopathia or vascular anomalies, and its measurement is indicated in patients with a suspected primary haemostatic defect when the platelet count is adequate. This test should not be performed if the patient is thrombocytopenic.



13.21 Macroplatelets can indicate platelet regeneration or may be breed associated, particularly in Cavalier King Charles Spaniels.
(Courtesy of T Stokol, Cornell University)



13.22 Evaluation of the buccal mucosal bleeding time is indicated to investigate primary haemostatic abnormalities when the platelet count is normal.

Prothrombin time and activated partial thromboplastin time: The prothrombin time (PT) and activated partial thromboplastin time (aPTT) evaluate secondary haemostasis. Samples are collected into plastic or siliconized glass tubes with 3.2% citrate as an anticoagulant at a ratio of 1:9 with the blood sample. If samples cannot be analysed within 12 hours, the plasma should be separated and frozen. The PT tests the extrinsic and the common pathways and thus evaluates factors VII:TF, X, V and II. Owing to the short half-life of factor VII, this test is very sensitive to vitamin K deficiency and is the test of choice in suspected anticoagulant rodenticide intoxications. The aPTT tests the intrinsic and common pathways, and is more sensitive than the PT to heparin and DIC. For PT or aPTT values to be prolonged, at least one factor must be decreased to below 30% of normal concentration. The aPTT is also commonly used to monitor therapeutic heparinization, but is also affected by heparin used for catheter locks or flushes. A discard tube should therefore be used when samples are collected from vascular catheters.

A point-of-care coagulometer (e.g. CoagDx, QuikVet) is an attractive alternative to conventional laboratory testing. Using citrated whole blood, reported sensitivity and specificity for diagnosis of PT prolongation are 85.7% and 95.5%, respectively (Tseng *et al*., 2001). That is, the test will not detect all anomalies of the extrinsic system, and a

small number of false positives occur. Using citrated whole blood, reported sensitivity and specificity for diagnosis of aPTT prolongation is 100% and 83%, respectively (Tseng *et al*., 2001). As such, it is an excellent screening test for abnormalities of the intrinsic and common pathways, with a small number of false positives. Abnormal results that do not correlate with clinical findings should be verified via conventional testing.

Activated clotting time: The activated clotting time (ACT) is a simple, point-of-care screening assay performed using non-anticoagulated whole blood. Negatively charged particulates, such as kaolin or celite, activate the contact pathway. As such, the ACT assesses the intrinsic and common pathways. It is less sensitive, and less specific, than the aPTT. The ACT is prolonged by severe abnormalities of the intrinsic and/or common pathways, but it is also affected by hypofibrinogenaemia, severe thrombocytopenia and by thrombopathia (including antiplatelet drugs). Like the aPTT, the ACT is sensitive to heparin. Several automated ACT assays are commercially available (iStat ACT+, Hemochron ACT for CoagDx).

Thrombin time: The thrombin time (TT) determines the reactivity of fibrinogen to exogenous thrombin. It assesses the conversion of fibrinogen to fibrin (the common pathway) and bypasses all other steps. It may be prolonged by hypofibrinogenaemia (<1 g/l), by dysfibrinogenaemia, or by substances that inhibit thrombin such as heparin or FDPs. Sample collection and handling are as for the PT and aPTT.

D-dimers: D-dimers are unique FDPs that are formed when cross-linked fibrin is lysed by plasmin. D-dimers indicate the activation of both thrombin and plasmin, and hence are more specific for active coagulation and fibrinolysis. D-dimers are a sensitive test for DIC and appear to be superior to traditional FDP assays for this purpose. However, they are not always elevated in patients with DIC, and elevated D-dimers are certainly not specific for DIC. They should be considered an ancillary diagnostic test, with the diagnosis of DIC relying on the appropriate constellation of clinical findings and abnormal results of haemostasis testing. D-dimers are also sensitive for thromboembolism in humans, and widely used as a screening test; however, the sensitivity may not be as high in dogs, and further studies are needed to characterize the diagnostic utility of D-dimers for diagnosis of thromboembolism in dogs. Several point-of-care D-dimer assays (Figure 13.23) have been validated in dogs, and these may be clinically useful in the emergency setting for patients with suspected DIC or thromboembolism (Dewhurst *et al*., 2008; Bauer and Moritz, 2009).



13.23 Evaluation of D-dimers at the point of care can aid the timely diagnosis of disseminated intravascular coagulation or thromboembolic disease. Several point-of-care assays have been evaluated for use in dogs, including the NycoCard D-dimer assay illustrated here. (Courtesy of D Chan, Royal Veterinary College)

Specialized coagulation testing

Platelet Function Analyzer: The Platelet Function Analyzer (PFA-100) is a point-of-care instrument that evaluates platelet function under arterial shear (Figure 13.24). It has been described as the *in vitro* equivalent of the BMBT (Jandrey, 2012). The PFA-100 aspirates citrate-anticoagulated blood through an aperture in a collagen membrane, coated with adenosine diphosphate (ADP) or adrenaline, under arterial shear. This leads to platelet activation, shape-change degranulation and adherence to the membrane. The closure time (CT) is recorded as platelet accumulation and plug formation occludes the aperture and prevents flow. The PFA-100 can be used to detect inherited, acquired or induced platelet dysfunction. The test, however, can be inaccurate in the presence of anaemia (Hct <35%), polycythaemia (Hct >60%) or marked thrombocytosis (>500,000 platelets/μl). The methodology lacks specificity and should be regarded as a screening tool to identify platelet hypofunction such that further testing can be better targeted. Clinical utility of the PFA-100 is limited by the need to perform the test shortly following sampling, and by the few institutions with this technology.

Platelet aggregometry: Light transmission aggregometry (LTA) using platelet-rich plasma remains the 'gold standard' for the clinical investigation of platelet function defects. The major benefit of the test is the ability to evaluate multiple platelet activation and signalling pathways through the use of various agonists over a range of concentrations. LTA enables the diagnosis of multiple primary platelet defects as well as evaluation of the efficacy of antiplatelet drugs. LTA is not widely available, however, and requires operator expertise and careful sample processing. Whole blood impedance aggregometry was developed as a point-of-care alternative to LTA. This analyser (Multiplate) has been validated for use in dogs (Kalbantner *et al*., 2010). It produces a single output value, rendering it more clinically useful. While experience with this methodology in small animals is currently limited, it may prove useful for both platelet function testing and the monitoring of antiplatelet medications.



13.24 Potential thrombopathias can be investigated at the point of care using specific platelet function analysers such as the PFA-100. This particular analyser enables testing of platelet aggregate formation under high-shear conditions and can evaluate several distinct pathways of platelet activation.

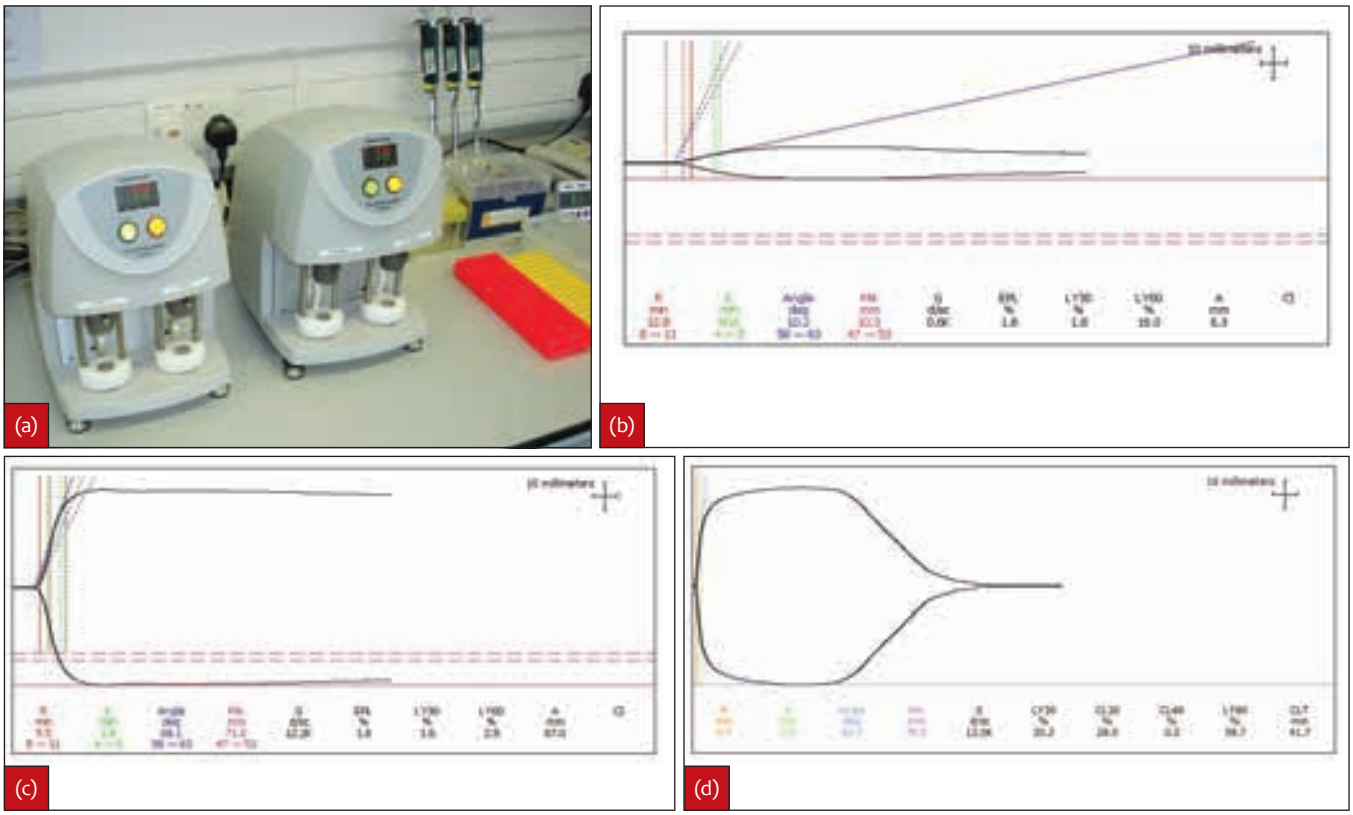
Thromboelastography and thromboelastometry: Whole-blood tests of coagulation such as thromboelastography (TEG) and thromboelastometry (ROTEM) evaluate the viscoelastic properties of blood during clot formation and lysis, and provide a global assessment of haemostasis that better reflects the *in vivo* cell-based model of haemostasis than conventional plasma-based haemostatic tests. Critically, TEG may be able to predict both haemorrhage and thrombosis in the clinical setting better than routine plasma-based assays. Both methodologies use a heated sample cup (37°C) into which the blood sample is placed, in some cases together with an activator or inhibitor. A plastic pin suspended from a detection system is placed into the sample cup, and the sample is cyclically oscillated relative to the pin. As coagulation progresses, the viscoelastic changes within the sample create torque forces on the pin. These are electrically transduced to a computer that generates a tracing, consisting of pre-coagulation, coagulation, and fibrinolysis zones (Figure 13.25). TEG and ROTEM provide comparable, although not identical, results (Wiinberg and Kristensen, 2010; McMichael and Smith, 2011). Numerous objective measurements are generated from the TEG tracing (thromboelastogram). The reaction time (R) measures the time to initiation of coagulation and evaluates primarily the 'intrinsic pathway'. The clot formation time (K), a measure of the speed of clot development, depends on factor VIII, thrombin and fibrin generation rates, platelet number and function, and Hct. The alpha angle (α), also reflects the rate of clot formation and is dependent on similar parameters to the K. Maximum amplitude (MA) represents the maximal clot strength and reflects platelet number and function, fibrinogen concentration and Hct. The clot elasticity value (G) is derived from the MA, and may be a more sensitive parameter for the detection of hyper- or hypocoagulability.

The major advantage of viscoelastic testing is the ability to integrate multiple components of the haemostatic system into an overall view of the haemostatic potential. As such, it is an ideal screening assay to determine hypo- or hypercoagulability and to guide the selection of further testing. In human bleeding patients, TEG-based algorithms have been used to guide therapy (Ak *et al*., 2009). A disadvantage of TEG and ROTEM is that the contribution of individual coagulation parameters can be hard to determine. Moreover, they do not detect platelet adhesion disorders. These assays are also very sensitive to pre-analytical and analytical variation such that they can be hard to standardize. To this end, guidelines have been developed to improve comparability of TEG/ROTEM-derived parameters between centres (Goggs *et al*., 2014). The need to perform TEG and ROTEM testing within 30 minutes after sample collection limits their use to the few institutions with the technology. The clinical utility of these tests in small animal patients is still undergoing evaluation and their place in the management of patients is not yet clear.

Disorders of primary haemostasis

Thrombocytopenia

Thrombocytopenia is the most common primary haemostatic defect encountered in small animals, and may be due to decreased platelet production, or increased platelet destruction, consumption or sequestration (Figure 13.26). Spontaneous bleeding generally does not occur until platelet counts are lower than 40 x 10^9/l, unless another concomitant bleeding disorder exists. Many animals tolerate lower counts without evidence of haemorrhage. Secondary haemostasis should be evaluated in all thrombocytopenic animals to exclude DIC or other combined defects. If these



13.25 Whole blood viscoelastic tests of coagulation such as (a) thromboelastography are increasingly used in veterinary emergency and critical care to screen for hypo- and hypercoagulability. These assays may also enable identification of fibrinolytic disorders. Characteristic thromboelastography traces of patients with (b) hypocoagulability, (c) hypercoagulability and (d) hyperfibrinolysis are illustrated here.

Quantitative platelet disorders (thrombocytopenia)

Decreased production:
- Drug-induced (oestrogen, chloramphenicol, cytotoxics)
- Immune-mediated megakaryocytic hypoplasia
- Viral (feline leukaemia virus)
- Chronic rickettsial disease
- Oestrogen-secreting neoplasm
- Myelophthisis (myeloproliferative disease)
- Myelofibrosis
- Cyclic thrombocytopenia (*Ehrlichia platys*)
- Radiation
- Idiopathic bone marrow aplasia

Increased destruction:
- Immune-mediated (IMTP)
  - Primary
    - Idiopathic
    - Evans-like syndrome (IMHA and IMTP)
    - Systemic lupus erythematosus
  - Secondary
    - Drugs
    - Tick-borne disease
    - Neoplasia
    - Bacterial infection
- Non-immune
  - Drug-induced
  - Ehrlichiosis
  - Rocky Mountain spotted fever
  - Dirofilariasis

Consumption/sequestration:
- Disseminated intravascular coagulation
- Microangiopathies
- Sepsis
- Vasculitis
- Splenic torsion, hypersplenism
- Hepatic disease
- Profound acute haemorrhage
- Haemolytic uraemic syndrome

Qualitative platelet disorders (thrombopathia)

Inherited:
- von Willebrand's disease (numerous dog breeds)
- Canine thrombopathia (Basset Hound)
- Canine thrombasthenic thrombopathia (Otterhound)

Acquired:
- Drug-induced (e.g. NSAIDs, synthetic colloid solutions, antibiotics)
- Uraemia
- Hepatic disease
- Pancreatitis
- Myeloproliferative disorders
- Dysproteinaemia (e.g. myeloma)
- Hypothermia

Vascular disorders

Inherited:
- Ehlers–Danlos syndrome

Acquired:
- Vasculitis
- Hyperadrenocorticism

13.26 Causes of primary haemostatic disorders. IMHA = immune-mediated haemolytic anaemia; IMTP = immune-mediated thrombocytopenia; NSAIDs = non-steroidal anti-inflammatory drugs.

tests are normal, and particularly where a CBC shows evidence of other cytopenias, a bone marrow aspirate or biopsy is indicated to evaluate platelet production.

Megakaryocytic hypoplasia can result from numerous conditions. In the absence of a compatible drug history, or evidence of myelophthisis or myelofibrosis on bone marrow examination, further testing should include investigation into potential neoplastic, infectious or immune-mediated aetiologies. Oestrogen-secreting tumours, chronic rickettsial disease (*Ehrlichia canis*) and viral infections such as FeLV and FIV should be considered where appropriate. Immune-mediated megakaryocytic hypoplasia can present a diagnostic dilemma as bone marrow megakaryocytes are decreased (Miller and Lunn, 2007). Diagnosis in these cases is usually by exclusion of other differentials and evaluation of the response to immunosuppressive therapy.

Normal or increased numbers of megakaryocytes in thrombocytopenic patients indicate increased platelet destruction, consumption or sequestration. Common causes of platelet consumption and sequestration include DIC, sepsis, vasculitis, splenic torsion and severe acute bleeding (e.g. anticoagulant rodenticide), which can often be excluded on the basis of clinical findings. As a general rule, most causes of consumptive thrombocytopenia lead to a mild or moderate decrease in circulating platelet numbers. Splenic torsion is an exception, occasionally causing a severely decreased platelet count. DIC may also occasionally result in profound thrombocytopenia, but is then associated with concomitant anomalies in secondary haemostasis.

Immune-mediated thrombocytopenia (IMTP) is the most common cause of severe thrombocytopenia in the dog, but is rare in the cat (Kohn *et al*., 2006). Definitive diagnosis of IMTP can only be achieved by the identification of antiplatelet immunoglobulins. It should be noted, however, that platelet surface-associated immunoglobulin occurs in other disease processes and hence this finding lacks specificity for IMTP. Since this detection is only available in a research setting, the clinical diagnosis of IMTP must be based on careful exclusion of other causes of thrombocytopenia. IMTP can be idiopathic, may be associated with other immune-mediated processes, such as IMHA or SLE (Goggs *et al*., 2008), or may develop secondary to drugs (notably sulphonamides), neoplasia (especially lymphoid), tick-borne disease, or infection. Suspicion of IMTP, therefore, should prompt a thorough search for underlying disease. In addition to a CBC, chemistry and urinalysis, diagnostic testing could include radiology or ultrasonography, a direct Coombs' test, an ANA test, Baermann faecal examination for *Angiostrongylus vasorum*, and serology for tick-borne diseases, occult dirofilariasis and, in the cat, viral diseases.

Management of IMTP includes the treatment of any underlying cause, adequate immunosuppression and appropriate supportive care. Glucocorticoids are the mainstay of immunosuppressive therapy: either prednisone/prednisolone (1–2 mg/kg orally q12h for animals <10 kg, and 15 mg/m^2 orally q12h for animals >10 kg) or dexamethasone (0.2–0.4 mg/kg i.v. q24h). The use of gastrointestinal protectants (omeprazole/pantoprazole) is recommended. When tick-borne disease is deemed possible, doxycycline is indicated (10 mg/kg orally or slow i.v. q24h). Response to glucocorticoid therapy, as evidenced by a significantly increased platelet count, generally occurs within 2–7 days. Both vincristine (0.02 mg/kg i.v. once) and hIVIG (0.5–1.0 g/kg slow i.v. infusion) have been advocated in dogs with IMTP to more rapidly restore platelet numbers (Rozanski *et al*., 2002; Bianco *et al*., 2009). While comparable efficacy has not been firmly established, vincristine is more cost-effective than hIVIG (Balog *et al*., 2013).

Thrombocytopenic patients can deteriorate rapidly due to massive haemorrhage (most commonly into the gastrointestinal tract) or due to haemorrhage into a vital organ, such as the lungs or brain. Transfusion of whole blood, platelet concentrates or dimethyl sulfoxide, stabilized frozen platelets is indicated for patients who have clinical signs suggestive of life-threatening haemorrhage secondary to IMTP, although routine use is limited by availability. Patients should be hospitalized until platelet counts exceed 50 x 10^9/l and bleeding has ceased. Thereafter, counts should be regularly monitored. When the platelet numbers are within the reference range, corticosteroid

dose is decreased by approximately 25%, and then tapered gradually over 3–6 months, with close monitoring of platelet counts. Relapses of thrombocytopenia during the corticosteroid taper occur in approximately 10% of cases and are unpredictable (O'Marra *et al*., 2011), necessitating periodic monitoring of the platelet count. If relapse occurs, the corticosteroid dose should be temporarily increased, and addition of an adjunctive immunosuppressive drug to the therapeutic regimen may be considered. Options in the dog include azathioprine, ciclosporin and mycophenolate mofetil, for cats, Ciclosporin is used (dosages are available in the immune mediated haemolytic anaemia section, above). Splenectomy is generally reserved for patients that have splenomegaly and exhibit refractory IMTP. Prior to splenectomy, it is crucial to rule out protozoal disease, and to ascertain (via bone marrow biopsy) that the spleen is not the primary source of extramedullary haematopoiesis.

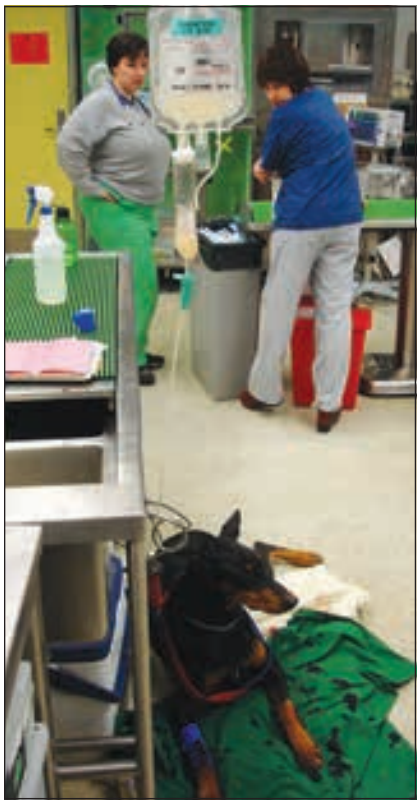
Thrombopathia

Vascular disorders are a relatively uncommon cause of bleeding. In patients with clinical evidence of a primary haemostatic disorder or a prolonged bleeding time and normal platelet numbers, a platelet function defect is likely. The patient's drug history should be carefully appraised because drugs are frequent causes of thrombopathia (see Figure 13.26). Numerous diseases can precipitate platelet dysfunction, including uraemia, hepatic disease, pancreatitis, myeloproliferative disorders and myeloma. Hypothermia, as results from hypoperfusion, evaporation from exposed body cavities during surgery, or the infusion of cold resuscitation fluids, leads to a reversible hypocoagulability, resulting primarily from decreased platelet adhesion. If no obvious cause of thrombopathia can be found, a hereditary disorder should be suspected. VWD is most common, and VWF can be readily assayed for confirmation. Other thrombopathias require specific platelet function testing, performed by specialist laboratories (Boudreaux, 2012).

Control of haemorrhage in the dog with VWD includes the administration of VWF in plasma products, and/or desmopressin acetate (DDAVP). Cryoprecipitate is the ideal plasma product, as it contains relatively large quantities of VWF (Figure 13.27). If cryoprecipitate is not available, fresh frozen plasma can be used. DDAVP (1 μg/kg s.c.) can result in increased VWF concentrations and a positive clinical effect in dogs with Type I VWD, but has a limited duration of action. It can be administered during a bleeding crisis or 20–30 minutes prior to an anticipated trauma such as surgery. Efficacy can be estimated by repeating a BMBT 30–60 minutes after administration. DDAVP has also been used successfully to control aspirin-induced thrombopathia in dogs (Di Mauro and Holowaychuk, 2013), and multiple platelet disorders in humans.

Disorders of secondary haemostasis

Defects of secondary haemostasis can be hereditary or acquired (Figure 13.28). Hereditary coagulopathies are quantitative disorders of specific coagulation factors, usually noted in purebred dogs (Barr and McMichael, 2012). These result in prolongation of the PT, aPTT or both, depending on the factor involved. Factor XII deficiency, common in cats, results in aPTT prolongation but, because factor XII is not an activator of coagulation *in vivo*, it is not associated with a bleeding disorder.



13.27 A Dobermann with von Willebrand's disease receiving a plasma transfusion in the emergency room. Transfusion therapy is frequently required in the treatment of bleeding disorders.

Inherited
Deficient factor: • I: Hypo/dysfibrinogenaemia (St. Bernard, Borzoi) • II: Hypoprothrombinaemia (Boxer) • VII: Hypoproconvertinaemia (Beagle, Alaskan Malamute) • VIII: Haemophilia A (numerous dog breeds, crossbreeds, cats) • IX: Haemophilia B (numerous dog breeds, British Shorthair cat) • X: Stuart Prower trait (Cocker Spaniel) • XI: Plasma thromboplastin antecedent deficiency (Springer Spaniel, Pyrenean Mountain Dog) • XII: Hageman factor deficiency (numerous dog breeds, cats)
Acquired
• Vitamin K deficiency/antagonism • Hepatic disease • Disseminated intravascular coagulation • Circulating anticoagulants (e.g. heparin)

13.28 Causes of secondary coagulation disorders.

Acquired coagulopathies include vitamin K deficiency or antagonism, hepatic disease, DIC and anticoagulants (e.g. heparin). Haemodilution, acidaemia and severe hypothermia also result in acquired coagulopathy in the critical patient. Acquired coagulopathies tend to affect multiple factors in both the intrinsic and extrinsic pathways. Factor VII has the shortest half-life (4–6 hours) so prolongation of the PT may precede aPTT prolongation in early vitamin K deficiency or acute hepatic failure. Conversely, the aPTT alone may be prolonged with heparin therapy, DIC or dilutional coagulopathy.

Anticoagulant rodenticide toxicity

Synthesis of vitamin K-dependent factors (II, VII, IX and X) occurs in the liver. Vitamin K is an essential cofactor for carboxylation of these proteins, rendering them functional. During this reaction, vitamin K is converted to an epoxide metabolite, from which vitamin K is recovered by vitamin K epoxide reductase (VKOR). The most common cause of

vitamin K deficiency in dogs is the ingestion of anticoagulant rodenticides. These toxins inhibit VKOR and thus interfere with vitamin K recycling and prevent the production of functional clotting factors. Clinical signs of a secondary haemostatic disorder generally occur 2–5 days after ingestion. Prolongation of the PT occurs first but, by the time haemorrhage is evident, the PT, aPTT (and ACT) are typically all prolonged. Fibrinogen concentrations, platelet counts and D-dimers are usually normal, but may be altered by bleeding. Toxicological testing for specific rodenticides is not usually helpful in the emergency situation, but may serve to confirm an uncertain diagnosis or to guide vitamin K therapy.

Vitamin K1 therapy is essential to management. Improved coagulation, however, requires the synthesis of new factors, which commonly takes up to 12 hours. As such, emergency needs for clotting factors can be met only by transfusion of plasma (recommended dose is 10–20 ml/kg). Fresh whole blood (20 ml/kg), or administration of both PRBCs and plasma, are indicated if the patient is anaemic. The half-life of transfused clotting factors is relatively short, thus plasma transfusion may need to be repeated. Decisions on the need for higher or repeat doses of plasma should be made following rechecking of the PT and aPTT. Parenteral administration of vitamin K1 (5 mg/kg q12h) is recommended for initial therapy, ideally subcutaneously to avoid iatrogenic haemorrhage. The intravenous route should be avoided due to the potential for anaphylaxis. After 24 hours, if the patient is not vomiting, vitamin K1 therapy is administered orally (0.25–2.5 mg/kg daily in warfarin exposure, and 2.5–5.0 mg/kg for long-acting rodenticides). Vitamin K1 has no effect on toxin elimination. Therapy must be maintained until the toxin has been metabolized. If the anticoagulant is known to be warfarin, 1 week of therapy is usually sufficient. If the anticoagulant is unknown or is a second-generation rodenticide, oral vitamin K1 should be continued for at least 3–4 weeks. The PT must be evaluated 48–72 hours after cessation of therapy. If it is prolonged, therapy should be reinstated for an additional 2 weeks and the PT again re-evaluated after discontinuation. In cases of uncertain rodenticide ingestion, or where early gastrointestinal decontamination can be instituted, it is acceptable to withhold vitamin K therapy pending a repeat PT test 48 hours after exposure. If the test is prolonged at this time, vitamin K therapy should be instituted, while no further therapy is required if PT is normal (Pachtinger *et al*., 2008).

Hepatic failure

Severe hepatocellular damage results in variable factor deficiencies and/or abnormalities in vitamin K metabolism (Prins *et al*., 2010). Both quantitative and qualitative platelet disorders can occur. FDPs and D-dimers may be elevated, and antithrombin (AT), and fibrinogen concentrations may be reduced (Kavanagh *et al*., 2011). Excessive fibrinolysis can result from reduced clearance of plasminogen activators and reduced synthesis of fibrinolytic inhibitors. Differentiation from DIC is sometimes impossible based on coagulation testing alone, and depends on clinical findings, serum chemistry parameters and liver function testing. Patients with hepatic failure frequently have gastrointestinal bleeding, which can precipitate hepatic encephalopathy. Bleeding tendencies must be corrected before pursuing hepatic biopsy or other invasive procedures. Transfusion of fresh frozen plasma can temporarily offset factor deficiencies. Vitamin K1 is beneficial in some patients; efficacy should be ascertained by repeating coagulation tests at least 12 hours after initiation of therapy.

Dilutional coagulopathy

Dilutional coagulopathy refers to the syndrome resulting from blood loss, consumption of coagulation factors and platelets, and intravascular volume replacement. During hypovolaemic shock, reduced intravascular volume results in shifts of factor-deficient interstitial fluids into the plasma. This is compounded by aggressive resuscitation with intravenous fluids and/or massive RBC transfusion, and further exacerbated by synthetic colloids. In human patients, 40–60% haemodilution produces a coagulopathy, and the coagulopathy increases with increasing fluid volumes.

Fibrinogen is the first factor to become critically reduced with haemodilution. Hypofibrinogenaemia decreases the speed, strength and stability of clot formation. This effect is seen with even moderate blood loss and haemodilution. The magnitude of the coagulopathy is determined by the severity of the hypofibrinogenemia and the type of resuscitative fluid used. Hydroxyethyl starch demonstrates the most pronounced haemodilution effects because it also affects VWF and factor VIII. Thrombocytopenia and the dilution of coagulation factors affect haemostasis at a later point in resuscitation than does hypofibrinogenaemia. After replacement of one blood volume of platelet-deficient fluid, only 35–40% of platelets remain in the circulation. In the patient with a normal platelet count before resuscitation, this dilution may not be clinically significant. In 15 massively transfused dogs, moderate thrombocytopenia was recorded in all dogs in which platelet counts were measured, but none developed counts below 50,000/μl (Jutkowitz *et al*., 2002). Prolongation of PT and aPTT occurs in human patients after replacement of two blood volumes. Prolongations were demonstrated in 70% of dogs after massive transfusion, but a correlation to transfused volumes was not made (Jutkowitz *et al*., 2002). The effects of haemodilution on haemostasis are further compounded by hyperfibrinolysis.

Dilutional coagulopathy is mitigated by the early use of plasma products and platelets in resuscitation protocols. Human studies suggest a beneficial role of fibrinogen transfusion (via cryoprecipitate or fibrinogen concentrate).

Disseminated intravascular coagulation

DIC refers to the intravascular activation of haemostasis with resultant microcirculatory thrombosis. Exaggerated consumption of platelets and coagulation factors ultimately results in defective haemostasis and a bleeding tendency. Fibrinolysis of microthrombi generates FDPs, further exacerbating the bleeding disorder.

DIC occurs secondary to a wide variety of underlying diseases, including sepsis, severe infections (viral, bacterial, parasitic and protozoal), neoplasia, shock, heat stroke, haemolysis, pancreatitis, severe hepatic disease, trauma and tissue necrosis. Three basic 'trigger' mechanisms have been proposed: activation of the extrinsic coagulation pathway by TF released during cell injury; contact activation of the intrinsic coagulation pathway via endothelial damage and exposure of the subendothelial matrix; and direct activation of coagulation factors by certain enzymes (e.g. trypsin in pancreatitis). Numerous factors can act as 'enhancers' of DIC. Acidosis and hypoxia increase endothelial damage and inhibit AT. Vascular stasis decreases the removal of activated coagulation factors and exacerbates local acidosis and hypoxia. The functional capacity of the mononuclear phagocytic system and the liver may be overwhelmed, hindering the removal of endotoxins, FDPs, enzymes and immune complexes.

The clinical manifestations of DIC vary depending on the inciting cause, the ability to replace depleted factors

and platelets, the concentrations of natural anticoagulants, and the efficacy of clearance of activated factors and FDPs. DIC can be subclinical, mild or severe, and acute or chronic. It can result in multiple organ failure due to microvascular thrombosis, or bleeding due to consumption of coagulation factors and platelets. Microvascular thrombosis is more common, leading to ischaemia, which can manifest as renal failure, respiratory insufficiency, hepatic failure, neurological defects or gastrointestinal disorders. Bleeding tendencies may manifest as disorders of primary and/or secondary haemostasis.

The diagnosis of acute fulminant DIC is usually easily made, while chronic or subclinical DIC may prove more difficult. Laboratory findings are extremely variable. Diagnosis of DIC, therefore, requires careful consideration of both the clinical and the laboratory findings, with no single finding being pathognomonic. The routine coagulogram identifies only those patients with fulminant DIC. Thrombocytopenia is almost invariably present but may be mild; relative changes may be undetected unless a recent platelet count is available for comparison. The PT, and more often the aPTT, may be prolonged, but both may be normal if compensatory factor production is adequate. Significant elevations of FDPs or D-dimers are highly suggestive of DIC, but are non-specific (Stokol *et al*., 2000). Schistocytosis is significant, but is not invariably present and may occur with other conditions. AT levels are decreased in most dogs with DIC. Fibrinogen concentrations are usually low, but may be normal or increased because fibrinogen is an acute phase protein. TEG is valuable for DIC diagnosis and can identify the more common hypercoagulable state (Wiinberg *et al*., 2010).

The treatment of DIC is fourfold:

- Correction of the underlying cause
- Optimization of perfusion via appropriate fluid therapy
- Prevention of secondary complications
- Control of the haemostatic defects.

Correction of the underlying cause must be the primary focus because, until it is reversed, haemostatic activation will continue. Fluid therapy is essential to remove activated clotting and fibrinolytic factors from the microcirculation and to maintain adequate tissue perfusion, thereby alleviating vascular stasis, tissue hypoxia and acidosis. The prevention or control of secondary complications includes the correction of acid–base and electrolyte disorders, supplemental oxygen therapy where indicated, the maintenance of adequate perfusion to prevent renal and gastrointestinal ischaemia, and the prevention of secondary sepsis. Control of the haemostatic defects of DIC can be attempted via blood product administration. Plasma transfusion provides AT and replaces depleted coagulation factors. If the patient is actively bleeding, fresh whole blood can replace RBCs, coagulation factors and platelets. The use of heparin in the treatment of DIC remains controversial (Ralph and Brainard, 2012) and is not currently recommended for overt (hypocoagulable) DIC where PT and PTT are prolonged. The judicious use of antithrombotic medications in hypercoagulable (non-overt) DIC patients is rational, but must be closely monitored. In theory, heparin inhibits coagulation, decreasing the rate of consumption of coagulation factors and preventing the transition from non-overt to overt DIC. Because the primary mechanism of action of heparin is via potentiation of AT activity, heparin is not effective unless adequate concentrations of AT are present. The importance of AT in the treatment of DIC has been demonstrated in human septic patients (Gando *et al*., 2013).

Hypercoagulation and thrombosis

Thrombosis is the deposition of a thrombus within the vasculature, resulting in tissue ischaemia. Fragmentation of the thrombus produces emboli that can obstruct remote sites. The term thromboembolism (TE) is used inclusively to refer to thrombosis and/or embolism. TE can be characterized as arterial (aortic, cerebral) or venous (pulmonary, portal, vena caval). Pulmonary thrombi are typically found in the pulmonary artery; however, these thrombi arise in the systemic venous circulation, dislodge and move through the circulatory system to eventually lodge in the pulmonary circulation;, the pathophysiology and aetiology are considered, to be venous. Hypercoagulability, or thrombophilia, is the propensity for thrombosis.

Pathophysiology

Thrombosis depends on three major risk factors (Virchow's triad): endothelial damage or dysfunction (vascular injury); impairment of blood flow (stasis); and alterations in blood constituents to promote coagulation (hypercoagulability). It is likely that the presence of more than one risk factor is required to cause *in vivo* thrombosis (Aird, 2007). Vascular injury leads to the exposure of subendothelial components, resulting in platelet adhesion and activation of the coagulation system. Factors causing vascular injury include trauma, catheterization, inflammation, neoplastic invasion, parasitic damage and amyloid plaque deposition. Vascular stasis retards the removal of activated coagulation factors and causes local hypoxia and vascular injury. Stasis results from hypovolaemia, shock, cardiac insufficiency, blood vessel compression, immobility and hyperviscosity. True hypercoagulability refers to a change in the coagulation system that can be caused by platelet hyperaggregability, excessive activation or decreased removal of coagulation factors, deficiencies of natural anticoagulants (AT, protein C), or defective fibrinolysis.

Platelet aggregation is controlled by the interplay between proaggregating substances released by the platelets (including thromboxane A2 (TXA2) and ADP) and antiaggregating substances produced by the endothelium (including prostacyclin, ADP-ase and nitric oxide). Disturbance in this balance can promote thrombosis. In humans, clonal thrombocytosis is associated with thrombosis, while secondary thrombocytosis, more commonly seen in small animals, is unlikely to confer a thrombotic risk (Schafer, 2004).

Secondary haemostasis is negatively regulated by a number of mechanisms including AT, protein C, and TF pathway inhibitor. These mechanisms operate to prevent thrombus formation in normal circumstances, and to limit and localize the formation of the haemostatic plug. If one or more of these mechanisms fails, thrombosis is favoured. AT is synthesized primarily in the liver. It binds to and neutralizes thrombin (factor IIa) and factors IXa, Xa, XIa and XIIa. The rate of neutralization is markedly increased by heparin. AT deficiency may result from decreased production, increased loss or consumption. Decreased production of AT can occur with hepatic failure, but thrombosis generally does not result because hepatic failure also leads to decreased production of clotting factors and, on balance, these patients have a tendency towards haemorrhage. A similar situation occurs with protein-losing enteropathy (PLE). In contrast, protein-losing nephropathy (PLN) permits selective loss of

smaller plasma proteins such as AT, creating an imbalance that favours hypercoagulability. DIC results in increased AT consumption. Protein C is a vitamin K-dependent anticoagulant that inactivates factors Va and VIIIa, suppressing thrombin production. Protein C deficiency has been identified in dogs with thrombosis (Bauer and Moritz, 2013).

The fibrinolytic system is extremely important in the pathophysiology of TE. In a normal animal, thrombi lyse spontaneously within hours. The presence of persistent TE therefore implies hypofibrinolysis. Studies in humans have shown defective fibrinolysis to be a contributing mechanism in all of the hypercoagulable states. The fibrinolytic system consists of plasminogen and the activators that convert plasminogen to plasmin. Plasmin causes dissolution of the fibrin clot. There are two physiological plasminogen activators, tissue-type plasminogen activator (TPA) and urokinase, and numerous inhibitors of these activators. Hypofibrinolysis can occur due to decreases in plasminogen or plasminogen activators, or due to increases in inhibitors. The most common mechanism appears to be an increase in plasminogen activator inhibitor (PAI-1).

In small animals, the term hypercoagulable state refers to an acquired disorder in patients with underlying systemic disease associated with an increased risk of thrombosis (Figure 13.29). In these diseases, the pathogenesis is generally multifactorial and complex. Inherited hypercoagulable states have not been reported in animals. While hypercoagulability represents a risk for TE, the actual incidence is variable and unpredictable. Retrospective studies of postmortem examinations in dogs and cats with PTE have shown that a large proportion of patients had more than one condition potentially predisposing to hypercoagulability. The likelihood of TE in patients with these conditions appears to be increased when the disease is severe, when a second hypercoagulable condition is present, and when other prothrombotic factors intervene (such as hypoperfusion, immobility, venous catheterization, tissue injury and/or inflammatory cytokines). For these reasons, TE is common in critically ill patients.

Most hypercoagulable states in animals result in either arterial or venous TE, although some disease processes are more highly associated with one *versus* the other. For instance, cardiomyopathy in cats is associated with arterial TE (ATE), while IMHA predominantly leads to venous TE, particularly PTE.

Disease process/ risk factor	Hyper-coagulable state	Vascular flow abnormalities/ stasis	Endothelial injury/ dysfunction
Corticosteroid administration	✓		
Diabetes mellitus	✓		
Dirofilariasis	✓		✓
DIC (secondary to other disease)	✓		
Endocarditis (tricuspid/pulmonic)	✓		✓
Feline infectious peritonitis	✓		✓
Hyperadrenocorticism	✓		
Hypothyroidism	✓		
IMHA	✓		?
Indwelling venous catheters		✓	✓
Myocardial disease	✓	✓	✓
Neoplasia	✓	✓	
Pancreatitis	✓		✓
Protein-losing enteropathy	✓		
Renal amyloidosis/PLN	✓		
Sepsis	✓		✓
Surgery/trauma	✓	✓	✓

13.29 Risk factors for thrombosis. DIC = disseminated intravascular coagulation; IMHA = immune-mediated haemolytic anaemia; PLN = protein-losing nephropathy.

Clinical signs

The clinical signs of TE depend on the site affected, the function of the ischaemic organ, the extent of vascular compromise and the ability of collateral circulation to compensate for the insult. Clinical signs vary from mild subclinical effects to life-threatening complications. Manifestations of PTE range from mild acute tachypnoea to severe dyspnoea, obstructive shock and death. Embolization of the central nervous system ('stroke') can cause a variety of acute neurological signs. Emboli related to cardiac disease in cats frequently lodge in the aortic bifurcation. Signs are peracute and the affected limb is painful, cool, paretic, pale and pulseless. In contrast, signs of aortic TE in dogs range from peracute to chronic, and chronic cases may demonstrate only lameness or paresis. Visceral arterial thrombosis results in acute abdominal pain, vomiting, diarrhoea and/or haematochezia. Renal TE may cause abdominal pain, haematuria or oliguria, vomiting and dysrhythmias. Splenic vein thrombosis is commonly an incidental finding, but is sometimes concurrent with portal vein thrombosis, which can be associated with abdominal pain and ascites (Laurenson *et al*., 2010; Respess *et al*., 2012). None of these signs is specific for TE. Diagnosis, therefore, frequently relies on a suspicion of TE and exclusion of other causes.

Diagnosis

Perhaps the most important aspect in diagnosis is an index of suspicion. TE should be included in the differential diagnoses for dyspnoea, abdominal effusion, intestinal compromise, acute abdomen, haematuria, hindlimb lameness, paresis or paralysis, and the acute onset of neurological signs.

The diagnosis of TE should include:

- Exclusion of other potential causes of the clinical signs
- Confirmation of the presence of a thrombus/embolus
- Laboratory evaluation of hypercoagulation
- Identification of underlying systemic disorders.

Depending on the site of TE, diagnosis can be difficult. Since signs of TE are non-specific, and confirmation is frequently elusive, exclusion of other possible causes for the signs is an important diagnostic step. Confirmation of the presence of TE depends on the site, but generally relies on imaging studies. Aortic, caval or visceral thrombosis can generally be recognized via ultrasonography and Doppler studies. Both PTE and cerebral TE require advanced imaging modalities that currently have limited availability. PTE can be confirmed via selective angiography or scintigraphy but it is likely that spiral computed tomography pulmonary angiography is the diagnostic modality of choice (Goggs *et al*., 2009). Cerebral TE may be evident on magnetic resonance imaging (MRI).

Confirmation of hypercoagulability

In some situations, imaging studies may not be feasible, due to limited availability or patient instability. In such cases, diagnosis rests on the exclusion of other causes, documentation of hypercoagulability (where possible) and evidence of the presence of an underlying disease that might cause a hypercoagulable state. The presence of hypercoagulability neither confirms nor predicts TE but is indicative of the possibility and, together with other compatible findings, enables the clinician to build the case for a diagnosis. Laboratory confirmation of hypercoagulability, however, is difficult. The routine coagulogram (PT, aPTT, platelet count) is not helpful in identifying hypercoagulability and is typically normal in the hypercoagulable patient. When thrombosis has occurred, the coagulogram may show evidence of consumption (e.g. thrombocytopenia, prolonged aPTT).

D-dimers: Increased D-dimer concentrations occur in dogs with TE (Stokol, 2003; Bauer and Moritz, 2013). Since D-dimers are specific for active coagulation and fibrinolysis, they are useful for detecting TE, but not thrombotic risk. The half-life of D-dimers, however, is short (approximately 5 hours). As such, they are most useful for the detection of acute TE. They are also not specific for TE, with elevated concentrations being found in dogs with neoplasia, hepatic disease, renal failure, cardiac failure, internal haemorrhage, DIC and following surgical procedures. In humans, D-dimers have a high negative predictive value for TE, and are extensively employed as a screening test for PTE. The utility of D-dimers in small animal patients is less clear, but may be similar. Sensitivities of 89–100% have been reported in dogs, using the standard ELISA test, a latex bead agglutination test (Accuclot D-dimer®, Sigma), and a canine-specific point-of-care test (AGEN canine D-dimer test®, Sigma). Reported specificity is approximately 70%. When semi-quantitative methods have been employed, specificity approaches 90%, with strong positive results (>1000 μg/l on latex agglutination) occurring only in patients with TE and with haemoabdomen. Based on the available data in dogs, it appears that TE can be considered unlikely if the D-dimer test is negative and clinical suspicion is low. TE is not, however, excluded by a negative D-dimer result, especially if the time period from the event to presentation is prolonged. A positive test should always be interpreted in the light of other clinical findings. If these support TE, further testing is indicated. A strong positive test, in the absence of intra-cavitary haemorrhage, is highly suggestive of TE.

Fibrin split products (FSPs), like D-dimers, tend to be increased with TE; however, they are less sensitive and specific for active coagulation and thus TE than are D-dimers.

Antithrombin and fibrinogen: AT deficiency is a useful measure of hypercoagulability in patients with diseases associated with AT loss (e.g. PLN). It is possible that the magnitude of decrease may enable thrombosis risk stratification. Based on extrapolations from humans, AT activity of 50–75% is associated with moderate risk, while activities below 50% markedly increase thrombosis risk. Low concentrations of AT have been correlated with thrombotic risk when AT deficiency is the primary mechanism for thrombosis (e.g. PLN). AT levels may also be decreased as a result of consumption during massive TE. Normal AT concentration or activity does not preclude hypercoagulability. AT measurement is available at specialized laboratories.

Fibrinogen is the substrate for the generation of fibrin by thrombin. Fibrinogen measurement is widely available through commercial laboratories, and has potential utility in predicting the risk of arterial and, possibly, venous TE. In humans, fibrinogen concentration is an independent risk factor for various thromboembolic conditions (de Moerloose *et al*., 2010). Fibrinogen is a positive acute phase protein; fibrinogen concentration trends with the degree of inflammation. Significant hyperfibrinogenaemia is associated with hypercoagulability and is seen in the hypercoagulable states that accompany IMHA, pancreatitis and sepsis. The majority of patients with TE, however, do not have hyperfibrinogenaemia.

Thromboelastography and thromboelastometry: Hypercoagulable patients produce characteristic TEG/ROTEM tracings (see Figure 13.25). On TEG, these patients typically have short reaction (R) and clot formation (K) times, steep angles (a), and/or large maximum amplitudes (MA). In human patients, TEG has been shown to predict thrombotic risk following surgery or trauma. It is unclear which (if any) of the TEG parameters best relates to thrombotic risk in veterinary patients. Moreover, multiple unrelated factors, such as Hct, fibrinogen concentration, sample handling and assay parameters, affect the TEG/ROTEM tracing. A recent study evaluating TEG in dogs with TE in various anatomical sites found that, although the G-values of dogs with TE were significantly higher than those of controls, in 50% of the dogs TEG tracings were classified as normocoagulable (Bauer and Moritz, 2013). This suggests that TEG alone may lack the discriminant power necessary to reliably diagnose TE. It is apparent that viscoelastic tests have a place in the diagnostic work-up of TE, but further work is needed to determine predictive protocols and parameters.

Identification of underlying disease

Because TE occurs almost exclusively secondary to one or more underlying conditions, any suspicion of TE should prompt a thorough search for these conditions. While their presence does not confirm TE, it provides further support for the diagnosis of TE when a definitive diagnosis is not possible. Identification of underlying disease is also essential for clinical management.

Treatment

Therapy should always include:

- Support of the affected organ system/s
- Prevention of thrombus propagation and recurrence.

A relatively small percentage of TE events are immediately fatal. Even in patients with disturbed fibrinolysis, some degree of reorganization and lysis occurs in the days following the event. Therefore, if the patient can be supported through the compromise, and further exacerbations can be prevented (secondary thromboprophylaxis) via the appropriate use of antithrombotics, survival may be possible. In some cases, the resultant organ dysfunction may be too great to survive using this approach. In other cases, thrombi may persist in spite of antithrombosis. In these scenarios thrombolysis may be considered.

Thrombolysis

Therapeutic thrombolysis is the administration of supraphysiological doses of plasminogen activators, systemically

or directly at the site of thrombosis, to accelerate plasmin generation and induce thrombus dissolution. These drugs are administered to effect rapid reperfusion through lysis of the thrombus, but are associated with significant risk, most notably systemic bleeding and reperfusion injury. Contraindications for thrombolytic therapy include active internal bleeding, hypertension, recent (within 2–3 weeks) surgery or organ biopsy, and gastrointestinal ulceration. Drugs available in the UK include urokinase, streptokinase and recombinant TPA (alteplase, reteplase and tenecteplase). These drugs have distinct pharmacokinetics, thrombolytic activities, and fibrin specificities, and so are not interchangeable.

In human patients, thrombolytic drugs are commonly used for arterial TE. In patients with PTE, however, use is limited to those with haemodynamic instability or ventricular hypokinesis. Veterinary experience with thrombolytics is very limited and is predominantly in the field of feline ATE, precluding generation of evidence-based recommendations. No consensus on their administration exists and clinicians must determine the potential benefits and risks of administration for individual patients (Lunsford and Mackin, 2007). Protocols that are both safe and effective have not been established. A recent prospective clinical trial of TPA in 11 cats with ATE highlighted the risks associated with these agents (Welch *et al*., 2010). Although efficacious in more than 50% of cats, all patients suffered adverse effects, many attributable to reperfusion injury. Recent advances in small animal interventional radiology may provide novel methods or routes for thrombolysis (Dunn, 2011). Thrombolytic therapy should only be considered in veterinary patients where continuous haemodynamic monitoring is available. In appropriate cases, fibrin-specific drugs with short half-lives (e.g. alteplase) are preferred.

Antithrombotic drugs

Thrombi tend to propagate, and this can result in further compromise. Furthermore, the patient with TE is always at risk for additional TE episodes. Management, therefore, should be focused on limiting propagation and preventing recurrence through the use of anticoagulants and/or antiplatelet drugs. Traditionally, anticoagulants have been recommended to prevent venous thrombosis, and antiplatelet drugs to prevent arterial thrombosis. This is based on extensive clinical research and experience in human patients. More recently, it has been shown that antiplatelet drugs may decrease PTE-associated morbidity and mortality when they are used together with anticoagulants. As such, there may be a role for antiplatelet therapy in addition to anticoagulants for patients with venous thrombosis (Lowe, 2006; Watson and Chee, 2008). Furthermore, since most hypercoagulable states in small animals can result in either venous or arterial thrombosis in an unpredictable fashion, the judicious concurrent use of anticoagulants and antiplatelet drugs has merit.

Anticoagulants: Traditional anticoagulation in veterinary patients has been with unfractionated heparin (UFH), although growing experience with low molecular weight heparins (LMWHs) and the recent generation of novel anticoagulants offer potential alternatives.

Unfractionated heparin: UFH is a heterogeneous mixture of polysaccharide molecules that bind to and enhance the ability of AT to inhibit thrombin (IIa) and factor Xa (although IXa, XIa and XIIa are also inhibited). The relative effect of heparin on these factors is dependent on its molecular size; smaller heparin molecules are unable to catalyse thrombin inhibition. UFH is inexpensive, widely available, and can be administered subcutaneously or intravenously. The bioavailability of subcutaneous UFH is extremely variable. Moreover, the drug is protein-bound, and breakdown is both dose-dependent and non-dose-dependent, resulting in varied and unpredictable dose-response relationships. Successful heparin therapy necessitates monitoring the anticoagulant response, and titrating the dose to the individual patient. Individually adjusted heparin dosing maximizes the efficacy of this drug while minimizing the potential for detrimental underdosing or excessive anticoagulation. This need for therapeutic monitoring reduces the cost-benefits of UFH, however, and there is no veterinary evidence that targeting any specific laboratory measure results in effective thromboprophylaxis. Therapeutic monitoring of heparin can be achieved using the aPTT, thrombin generation, viscoelastic testing, or anti-factor Xa levels. The therapeutic range of heparin, extrapolated from humans, is a concentration of 0.3–0.7 IU/ml by anti-factor Xa assay, but the assay is not widely available. Monitoring of the aPTT (or ACT) is more feasible, targeting an aPTT range of 1.5–2.0 times baseline. For the treatment of venous TE, intravenous UFH therapy is initiated with an intravenous bolus, followed by a continuous rate intravenous infusion, and titrated based on aPTT monitoring (Figure 13.30). Because AT is required for heparin effect, concurrent plasma transfusion may be necessary for patients with documented or suspected AT deficiency.

Subcutaneous administration of UFH is not recommended for initial therapy since is it rare to achieve aPTT values within the target range in a timely fashion. Hence, the use of subcutaneous UFH in patients with acute TE should be considered only where intravenous UFH or LMWH is not feasible. Published doses vary enormously. The authors use a dose of 300 IU/kg subcutaneous q6–8h, with adjustments based on regular aPTT determinations. There is limited evidence regarding the efficacious use of UFH in cats, and indications that aPTT results do not reliably correlate with plasma heparin concentrations in this species. For this reason, the authors prefer the use of LMWH in cats.

Low molecular weight heparins: LMWHs are manufactured from UFH to yield smaller molecules. Like UFH, LMWHs interact with AT to inhibit coagulation factors. The shorter average chain length of the polysaccharides in LMWHs limits the inhibition of thrombin, such that these drugs

aPTT	Dose change IU/kg/h	Additional action	Repeat aPTT
<1.2 x mean normal (baseline)	+4	Bolus 80 IU/kg	+6 h
1.2–1.5 x mean normal (baseline)	+2	Bolus 40 IU/kg	+6 h
1.5–2.0 x mean normal (baseline)	0	None	+6 h then q24h
2.0–3.0 x mean normal (baseline)	–2	None	+6 h
>3.0 x mean normal (baseline)	–3	Stop infusion for 1 hour	+6 h

13.30 Unfractionated heparin dosing. An intravenous bolus of unfractionated heparin at 80–100 IU/kg is administered, followed by a constant rate infusion of 18 IU/kg/h. Activated partial thromboplastin time (aPTT) is evaluated 6 hours after initiation of therapy. The aPTT is compared with the mean value of the normal range for that laboratory, or with the pretreatment value for that patient. Adjustments are given in the table.

have 2–3 times the activity against factor Xa compared with factor IIa. LMWHs bind less avidly to plasma proteins, compared with UFH, providing superior bioavailability and pharmacokinetic predictability, which results in enhanced safety profiles. Their onset of action is rapid, with peak effects generally seen at 2–4 hours. Several LMWHs are commercially available, including dalteparin and enoxaparin, each with distinct pharmacodynamics.

The aPTT cannot be used for LMWH monitoring. Monitoring of LMWH therapy is best achieved using an anti-factor Xa assay. In human patients, target therapeutic range is a peak anti-factor Xa concentration of 0.3–0.7 IU/ml, and this is extrapolated to small animals, though supporting evidence is lacking. TF-activated TEG may also be useful for dalteparin monitoring. Unfortunately, neither of these tests is widely available. As such, monitoring of LMWH therapy is not easily achieved, and dosing in these scenarios is empirical.

LMWHs are widely used in human patients for both primary and secondary thromboprophylaxis, and have been shown to be effective in experimental animal models, but published evidence of efficacy in veterinary patients is lacking. For secondary thromboprophylaxis in the patient with TE, LMWHs can be considered as an alternative to intravenous UFH and preferable to intermittent subcutaneous UFH. Based on current knowledge, the authors recommend a starting dose of dalteparin of 150 IU/kg s.c. q8–12h in the dog, and 150–180 IU/kg s.c. q8–12h in the cat. A suggested starting dose of enoxaparin is 1 mg/kg s.c. q12h in the dog and cat. Peak anti-factor Xa activity is measured 3–4 hours post-administration, and the dose adjusted accordingly. Once an effective protocol is established for the patient, continued monitoring appears unnecessary, except for patients in renal failure.

Antiplatelet drugs: Antiplatelet drugs should be initiated as soon as is feasible following ATE. They can also be considered as adjunctive thromboprophylaxis in patients with venous TE. This adjunctive effect has been demonstrated in human patients. Moreover, because most hypercoagulable states in animals can result in both venous and arterial thrombosis, there should be ongoing concern for the potential for ATE in these patients.

Aspirin: The prostaglandin synthase (COX) inhibitor aspirin (acetylsalicylic acid) irreversibly inhibits platelet synthesis of TXA2. Aspirin also inhibits the endothelial production of the platelet inhibitor prostacyclin but this is limited by the greater COX-1 *versus* COX-2 effects of aspirin and the ability of the endothelium to resynthesize prostacyclin. The antiplatelet effects of aspirin are extremely rapid, within 1–2 hours of oral administration.

Aspirin is the mainstay of thromboprophylaxis in human patients with atherosclerotic disease. The optimal indications and dosing protocols for aspirin in small animals are not known. The dose required to cause *in vitro* inhibition of canine platelet function varies with the assay used, but is in the range of 0.5–20 mg/kg. This wide range may be related to heritable variability in canine thromboxane responsiveness. A recent study suggested that 1 mg/kg q24h aspirin consistently inhibited platelet function in only a third of dogs. The use of low-dose (0.5 mg/kg q24h) aspirin has been recommended for primary thromboprophylaxis in dogs with IMHA. It should be noted, however, that this protocol is based on a single retrospective study (Weinkle *et al*., 2005) that suggested a survival benefit associated with low-dose aspirin administration. This has not been confirmed by other studies.

In cats, a dose of 81 mg/cat q72h has been traditionally used during management of ATE, but a low-dose protocol of 5 mg/cat q72h was shown to be equivalently effective with fewer adverse effects. A recent study suggested that cats with ATE that received clopidogrel survived on average 8 months longer than cats that received aspirin (Hogan *et al*., 2015). As such, clopidogrel may replace aspirin as the drug of choice for these patients. It should be noted, however, that the study did not evaluate the combination of both drugs, which is the standard of care in humans with acute coronary syndromes (Anderson *et al*., 2007).

Clopidogrel: ADP receptor antagonists, such as clopidogrel, inhibit the autocrine and paracrine positive feedback loops via $P2Y_{12}$ that are critical for the stabilization of platelet-rich arterial thrombi. Clopidogrel is a prodrug that is activated by hepatic cytochrome P450 metabolism. Platelet inhibition occurs within 24 hours of administration in dogs (Brainard *et al*., 2010). Pharmacokinetic studies of clopidogrel suggested this drug behaves similarly in dogs as in humans, and may be an effective antiplatelet agent in this species. Two recent studies have investigated the use of clopidogrel for primary thromboprophylaxis in dogs with IMHA (Haviland *et al*., 2009; Mellett *et al*., 2011). Neither study was able to demonstrate a benefit of clopidogrel, but both studies were likely underpowered. It is also worth noting that use of antiplatelet agents alone for thromboprophylaxis in IMHA, a disease characterized by venous TE, is questionable.

GPIIb/IIIa antagonists: The parenteral GPIIb/IIIa inhibitors abciximab, eptifibatide and tirofiban, which antagonize the platelet fibrinogen and VWF receptor, have been used in canine experimental models of myocardial infarction and coronary stent thrombosis. All three drugs effectively inhibit canine platelet aggregation in this setting but, to date, none has been used clinically in veterinary medicine. Barriers to their clinical use include cost, risk of haemorrhage, and the need for administration by continuous infusion. Eptifibatide causes fatal cardiotoxicity in cats, and should not be used in this species.

Primary thromboprophylaxis

The morbidity and mortality rates of TE are substantial. Moreover, diagnosis is difficult, and treatment of TE is frequently unsuccessful. This makes prevention imperative in the patient at risk. Prevention should address all aspects of Virchow's triad. This includes:

- Minimizing vascular stasis by maintaining adequate perfusion
- Minimizing vascular injury by the appropriate handling of venous catheters
- Altering the haemostatic system via the appropriate use of drugs.

Antithrombotic drugs are indicated when there is significant risk of TE. Assessment of TE risk in veterinary patients remains largely subjective. Understanding the risk factors in patient groups and in individual patients forms the basis for risk determination. The most convincing evidence of risk is a prior TE event. In many patients, multiple risk factors are present, and the risks are cumulative. Such a situation should therefore prompt consideration of prophylaxis.

The authors most frequently consider administration of antithrombotic therapy in feline cardiomyopathy with atrial enlargement, canine IMHA, severe acute pancreatitis, sepsis and PLN. Risk stratification, however, is subjective,

and based on the severity of disease and concomitant risk factors. AT concentrations, TEG tracings and D-dimers may assist in identifying at-risk patients or those in which TE may be occurring. Patients with uncomplicated hyperadrenocorticism or diabetes mellitus appear to have a low incidence of TE, and the need for prophylactic drugs in these patients is doubtful. The risk increases, however, when another thrombophilic condition is added, such as hypertension, PLN or surgery.

The choice of drug for primary thromboprophylaxis depends on whether TE risk is considered to be venous or arterial, the anticipated duration of therapy, and the compliance and finances of the owner. Options generally include subcutaneous UFH, LMWH, warfarin and the oral antiplatelet agents.

Prophylaxis for venous TE is usually initiated with LMWH or with subcutaneous UFH. Recommended doses of UFH in this scenario range from 150 to 250 IU/kg s.c. q8–12h. These doses seem unlikely to result in major haemorrhage, but the efficacy of this regimen has not been demonstrated, and it is considered unlikely to be reliably effective.

Warfarin is most commonly used for long-term outpatient thromboprophylaxis. It is an oral vitamin K antagonist, thus inhibiting the activation of vitamin K-dependent factors. Due to the half-lives of these factors, the anticoagulant effect of warfarin is not immediate. During the first 24–48 hours of therapy, only factor VII and protein C are significantly affected. Inhibition of protein C leads to a thrombotic tendency, before other factors are inhibited. For these reasons, heparin therapy should always overlap warfarin for at least the first 2 days, and until therapeutic levels of warfarin are achieved. Warfarin is initiated at a dose of 0.05–0.1 mg/kg orally q24h in the dog and the cat. A therapeutic range is generally achieved within 5–7 days. Therapy is monitored by use of the PT, and the calculated international normalization ratio (INR). The therapeutic range for warfarin is an INR of 2.0–3.0. Due to the risk of haemorrhage, and the influence of diet, comorbidity and administration of other drugs, close continued monitoring of warfarin therapy on an outpatient basis is essential.

LMWHs are an attractive alternative to warfarin. They are less frequently associated with haemorrhage and, after the initial establishment of an effective dose, do not require ongoing monitoring. Since their onset of action is rapid, thromboprophylaxis can be initiated with LMWHs, or UFH can be discontinued when LMWH therapy is initiated. These benefits contribute to offsetting the costs of these drugs. Doses are as outlined above for secondary thromboprophylaxis. Until effective dosing protocols are established in small animals, however, initial dose adjustments based on anti-factor Xa assay or TF-TEG are recommended.

Novel anticoagulants may ultimately provide alternatives to traditional anticoagulants. Rivaroxaban is an oral, direct factor Xa inhibitor, developed as a safer alternative to warfarin. Monitoring is via PT or aPTT. Rivaroxaban has recently been approved for PTE treatment in humans. Pharmacokinetics have been studied in dogs, and it is reportedly an effective anticoagulant in this species, but clinical experience is limited.

The oral prodrug dabigatran etexilate is a potent, reversible direct thrombin inhibitor. This class of drug does not require AT as a cofactor for anti-IIa activity and these drugs are also able to inhibit thrombin bound to the formed thrombus. Dabigatran is monitored via the PT, aPTT or the preferred ecarin clotting time (ECT). Dabigatran is approved for human use, but use in animals is not yet reported.

Antiplatelet drugs are clearly indicated for arterial thromboprophylaxis in diseases associated almost exclusively with arterial thrombosis (e.g. atherosclerosis, feline ATE). They also have benefit as adjunctive therapy in other hypercoagulable states. They could be considered as sole therapy for venous thromboprophylaxis where anticoagulant therapy is not feasible. Low-dose aspirin inhibits platelet function in dogs, but its effects may be limited and inconsistent (Brainard *et al*., 2007; Blois *et al*., 2010; Sharpe *et al*., 2010; Dudley *et al*., 2013). In dogs, clopidogrel may provide more consistent antiplatelet effects than aspirin (Brainard *et al*., 2010), while in cats with ATE the use of clopidogrel instead of aspirin may provide a survival benefit. The combination of aspirin and clopidogrel is standard of care for humans with acute coronary syndromes (Guyatt *et al*., 2012) and a combined TE risk of >20%. Since these two drugs have distinct but synergistic inhibitory effects on platelet function (Wiinberg *et al*., 2012), the combination may also prove to be of value in some veterinary patients considered to be at high risk.

Thromboprophylaxis should be continued until the risk of TE is considered sufficiently decreased. In patients with short-term reversible causes, such as pancreatitis, therapy for 1–2 weeks following clinical recovery is likely to be adequate. In patients with ongoing risk, such as IMHA, antithrombotic therapy is continued until the patient is weaned off corticosteroids. Indefinite therapy is recommended in patients with recurrent TE, or TE complicating malignancy or cardiac disease.

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Chapter 14

Transfusion medicine

Gillian Gibson and Mary Beth Callan

Transfusion medicine has become an essential part of modern small animal veterinary practice, reflecting the advancing knowledge and capabilities of general practitioners, referral hospitals and emergency clinics in managing critically ill and emergency patients. Historically, whole blood (drawn directly from the donor with use of anticoagulant) has been used in veterinary medicine and is usually administered to the recipient within hours of donation. However, with increased need for and use of blood, coupled with a limited supply, administration of blood components (e.g. packed red blood cells (PRBCs), plasma, platelet concentrate, cryoprecipitate) meets the specific transfusion need of a patient and is a more economical use of this precious resource.

In the UK, significant changes in veterinary guidance and legislation over the past several years have provided an opportunity for the development of in-house and commercial blood banks. The Royal College of Veterinary Surgeons (RCVS) has issued supporting guidance for veterinary surgeons (veterinarians) regarding blood collection and storage. The most recent guidance states 'taking blood from healthy donors with the permission of the owner and with the intention of administering the blood or its products to a recipient is recognised veterinary practice where there is an immediate or anticipated clinical indication for transfusion. Such a clinical procedure would be acceptable on the scale of an individual veterinary practice or between other practices in the locality' (https://knowledge.rcvs.org.uk). Non-food animal blood banks may apply for authorization from the Veterinary Medicines Directorate (VMD) to collect, store and supply blood for use in non-food-producing animals to meet unforeseen or exceptional needs.

As all blood must be sourced from healthy donors, there is an increased need for donor animals. A practice can increase its donor pool by actively recruiting suitable candidates, and screening for blood type in advance of need. Client evenings or veterinary staff visits to breed or training club meetings, information displays in reception areas, and local newspaper articles can increase public awareness about the need for canine and feline donors, often leading people to volunteer their animals for donation. Volunteer-based donor schemes rely on the altruism of the pet owner, with direct rewards usually being a bag of pet food or toys for the donor.

Knowledge and practice of appropriate blood collection, processing, storage and administration methods are essential for ensuring the safety of the donor and recipient, as well as maximizing the use of limited clinical resources.

Donor selection

Canine blood donors

Canine donors should be healthy, well tempered, large breed dogs weighing at least 23 kg to allow for collection of 450 ml of blood in standard human blood bags. Many blood donor programmes set an age range for donors of between 1 and 8 years, with use of dogs older than the upper age limit at the discretion of the veterinary surgeon after careful evaluation of the donor. The dogs should receive routine veterinary preventative healthcare, including vaccination according to practice protocols. Blood should not be taken within 10–14 days of having received a vaccine, or from any donor that has had surgery or been treated for medical illness within 3 months. Donors should not be receiving any medication at the time of donation with the exception of ectoparasite preventatives, routine worming medication or heartworm prophylaxis. As blood is most frequently obtained from the jugular vein, consideration should be given to the conformation of the dog and venous access. According to criteria published by the VMD, as agreed with the UK Home Office and the RCVS, dogs donating as part of an authorized blood bank programme must not be sedated to facilitate donations. If donations are being carried out in practice for immediate use, then light sedation may be used at the discretion of the veterinary surgeon; however, wherever possible sedation should be avoided. Therefore, it is important to choose a dog of suitable temperament that will remain still with minimal restraint during the blood collection procedure. Any dog that has previously received a transfusion may have developed alloantibodies against differing blood types and is unsuitable as a donor. In the past it was advised not to use bitches that had whelped because of the potential risk of the bitch becoming sensitized to different red blood cell (RBC) antigens during pregnancy. However, a recent study found no evidence of pregnancy-induced RBC alloantibodies in dogs (Blais *et al*., 2009). Nevertheless, to prevent any possible untoward effects of stress on a bitch and her fetuses/puppies, a currently pregnant or recently whelped bitch, or a bitch nursing puppies, should not be used as a blood donor.

Pre-donation tests for canine donors include determination of blood type (at a minimum dog erythrocyte antigen (DEA) 1 status), yearly haematology and general biochemistry profiles, as well as screening for infectious diseases endemic to their region or to a geographical location where they have previously lived. The risk of infection

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of any given donor depends on infectious disease prevalence and exposure of the potential donor to the infectious agent. Blood-borne pathogens that have the potential to be transmitted by blood transfusion include *Babesia* spp., *Ehrlichia* spp., *Anaplasma* spp., *Bartonella* spp., haemoplasma spp., *Leishmania* spp., *Brucella canis*, *Trypanosoma cruzi*, *Neorickettsia risticii* and *Rickettsia felis*. Screening for blood-borne pathogens that may have an impact on the health of the donor (even though they may not be transmitted to the recipient) is also an important consideration, and *Dirofilaria immitis* screening is routine in donors that live in endemic regions. As knowledge develops, other blood-borne pathogens may be added to this list. Updated guidelines for the screening of canine and feline blood donors for blood-borne pathogens were published as a consensus statement from the American College of Veterinary Internal Medicine (ACVIM) in 2016 (Wardrop *et al*., 2016).

Many of the blood-borne pathogens are vector-borne and are not currently endemic in the UK. In the UK, excluding dogs that have travelled outside of the UK currently prevents the need for exhaustive blood-borne pathogen screening; however, veterinary surgeons are encouraged periodically to review their policies, as pathogen prevalence within any donor population may increase with greater pet travel and changing global climates. Although the cost of testing should be considered, the safety of the blood transfusion is paramount, and appropriate testing of a donor should not be compromised for financial reasons.

In the UK, an emerging infectious agent of importance is *Angiostrongylus vasorum*. In addition to being a threat to the general health of the dog, occult coagulation abnormalities associated with *A. vasorum* infection may not become apparent until significant tissue trauma (e.g. surgery, injury) is induced. In an affected blood donor there would be an increased risk of jugular vein haematoma formation, or failure of cessation of haemorrhage from the donor venepuncture site. Testing for this disease using a point-of-care antigen test or routine prophylactic licensed treatment may be considered prior to blood donation, especially in areas where the disease has a high incidence.

Feline blood donors

Feline donors should be clinically healthy cats aged 1–8 years, receiving routine veterinary preventative healthcare, and weighing at least 4.5 kg. Unlike canine donors, cats usually require sedation for the donation; however, they should still be of an agreeable temperament to allow transportation to the veterinary surgery and handling for administration of the sedative. Given the problems with naturally occurring RBC alloantibodies in cats (see Feline blood types), it is essential that all feline donors, as well as recipients, be blood typed prior to collecting blood to prevent incompatibility of mismatched transfusions. To ensure that the feline donors are in good health, haematology, serum biochemistry and blood-borne pathogen screening for feline leukaemia virus (FeLV) (serology), feline immunodeficiency virus (FIV) (serology) and haemotropic mycoplasmas (polymerase chain reaction, PCR) are evaluated each year. The updated ACVIM guidelines for screening of feline donors for blood-borne pathogens also recommend testing for *Anaplasma phagocytophilum* and *Bartonella henselae*, and optimally including *Cytauxzoon felis* and *Ehrlichia canis*, particularly if there are known infections with these pathogens in their area or exposure to vectors (Wardrop *et al*., 2016). Cats that are positive for any blood-borne pathogen should not be used as donors. Furthermore, to have confidence in maintaining a negative disease status, it is preferable to use only cats that are confined to living indoors. If outdoor cats are used as blood donors, pathogen screening should be performed prior to each donation. However, given that testing might be performed prior to seroconversion and PCR and serology are not 100% sensitive in identifying infections, use of outdoor cats with greater exposure to pathogens still poses a risk to recipient cats despite more frequent screening.

Given the need for sedation in donor cats and the stringent requirements for prevention of transmission of blood-borne pathogens, it is often difficult to develop a large pool of feline donors. Some larger veterinary facilities choose instead to house a colony of disease-free donor cats, which after a period of service are re-homed as pets. Veterinary surgeons in the UK seeking to establish a donor colony should consult the Home Office and the RCVS regarding legal requirements.

General considerations

In addition to the yearly comprehensive health examinations, a complete donor history, physical examination, and packed cell volume (PCV) or haemoglobin (Hb) level should be performed prior to every donation to safeguard the health and assess the suitability of the donor.

Blood types

RBC types are determined by species-specific, inherited antigens present on the cell surface. Blood type incompatibility is observed clinically as transfusion reactions or neonatal isoerythrolysis, the occurrence and severity of which is variable between individuals and species. The frequency of canine and feline blood types varies with geographical location and breed, and although the published population incidence of various blood types may offer the veterinary surgeon guidance, it is based on surveys with limited animal numbers and may not be applicable to the individual animal in question.

Canine blood types

There are many systems used to describe the blood groups in dogs, though the DEA nomenclature is most widely in use in the current literature. Typing antisera exist for 4 DEAs (1, 4, 5, and 7). Typing antisera for DEA 3 is no longer available. For all of the DEA groups a dog may be positive or negative. DEA 1 is a complex blood group system with varied surface expression levels, resulting in dogs testing either negative or weakly to strongly DEA 1 positive on blood typing kits (Acierno *et al*., 2014; Polak *et al*., 2015).

The relevance of a blood type is related to its antigenic potential. The most antigenic blood type is DEA 1. Dogs do not have clinically significant naturally occurring alloantibodies to other blood types. As such, most dogs will not experience a severe reaction during their first transfusion, even if administered RBCs of a different blood type. However, sensitization will occur; most significantly, in DEA 1-negative dogs receiving DEA 1-positive cells, antibodies (strong haemolysins and agglutinins) are produced, which can cause an acute haemolytic transfusion reaction after repeated antigen exposure (i.e. a second transfusion with DEA 1-positive blood). Production of antibodies to RBC antigens may develop in a sensitized recipient as early as 4 days after transfusion, emphasizing

the importance of performing a blood crossmatch prior to a second RBC transfusion beyond this time.

The significance of transfusion incompatibility associated with RBC antigens DEA 3, 5 and 7 varies, depending on the clinical consequences of a type-mismatched transfusion, as well as the prevalence of these antigens in the dog population. Naturally occurring anti-DEA 3, anti-DEA 5 and anti-DEA 7 antibodies have been documented but have not yet been associated with acute haemolytic transfusion reactions. However, sensitization to these RBC antigens or the presence of naturally occurring alloantibodies may result in a delayed transfusion reaction involving sequestration and loss of transfused RBCs within 3–5 days post-transfusion.

Prevalence studies in the USA report a low incidence of both DEA 3 and 5, with naturally occurring alloantibodies documented in 10–20% of dogs negative for these types. However, approximately 50% of dogs express the DEA 7 antigen, with an estimated 20–50% of the DEA 7-negative dogs having weak, low-titre non-haemolytic anti-DEA 7 antibodies (Andrews and Panedo, 2010). Thus, DEA 7 may bear more significance than other blood types, with the exception of DEA 1, with regard to premature removal of transfused RBCs from the circulation.

Blood type DEA 4 is a high-frequency antigen, with an estimated 98% of dogs being DEA 4-positive. Some blood banks define the 'universal' canine donor as being positive for DEA 4 and negative for DEA 1, 5 and 7. There is no known naturally occurring alloantibody to this antigen. However, there is a single case report of a DEA 4-negative dog sensitized by previous transfusion that experienced an acute haemolytic transfusion reaction after administration of DEA 4-positive blood, highlighting the fact that there is no true 'universal' canine blood donor (Melzer *et al*., 2003).

High-frequency or common RBC antigens pose a significant challenge in the management of sensitized dogs lacking these antigens, which are at risk for acute haemolytic transfusion reactions (Callan *et al*., 1995; Blais *et al*., 2007) if they require more than one transfusion. The failure to obtain a compatible crossmatch with several blood donors (DEA 1-negative or of the same DEA 1 type as the recipient) should prompt the clinician to consider that the patient has an alloantibody to a common RBC antigen and that a sibling, if available, may be a compatible source of blood; there is a one in four chance that a sibling will be homozygous for the allele encoding for a lack of the RBC antigen. Novel blood groups not described by the DEA system are still being identified. For example, in the case of the *Dal* antigen, a Dalmatian (*Dal*-negative) transfused with *Dal*-positive blood was sensitized, resulting in an inability to find crossmatch-compatible RBCs among 55 donors tested; however, four of 25 unrelated Dalmatians, also lacking the *Dal* antigen, were determined to be crossmatch-compatible (Blais *et al*., 2007). The prevalance of the Dal-positive blood type among donor dogs in North America is high (~97%). However, in addition to Dalmatians, Doberman Pinschers were found to have a higher percentage of Dal-negative blood type (42%), indicating that Doberman Pinschers could be a source of compatible blood for Dal-negative recipients previously sensitized to the Dal antigen (Goulet *et al*., 2017). The finding of additional RBC antigens outside of the familiar DEA system demonstrates the importance of considering other potentially significant blood type incompatibilities not identified by current commercially available typing methods and highlights the importance of the blood crossmatch to detect such incompatibilities in previously transfused dogs.

Traditionally, blood typing methods have been based on an agglutination reaction in which antigens are detected by visualizing haemagglutination in response to polyclonal or monoclonal antibodies. When using these antibodies, agglutination detects the presence of the particular RBC antigen being tested, and the dog is then considered positive for that antigen. Lack of haemagglutination in response to the antibody indicates that the dog is negative for the test antigen. Due to the subjective interpretation of haemagglutination reactions, more recently an immunochromatographic-based assay has been developed for in-practice typing for DEA 1. In addition, a flow cytometric method has been developed for detection of the DEA 1 antigen. As DEA 1 is the most antigenic blood type, it is strongly advised that the DEA 1 status of both the donor and recipient is determined prior to transfusion.

Typing for antigens other than DEA 1 requires the use of polyclonal antisera, available from only a few specialized blood service laboratories. Ideally, a donor would be negative for DEA 1, 5 and 7. As a general rule, DEA 1-negative dogs should only receive DEA 1-negative blood, and DEA 1-positive dogs may receive either DEA 1-negative or -positive blood. Subsequent potential incompatibilities to known or as yet undetermined RBC antigens in animals previously transfused should be identified on a crossmatch.

The card test kits for DEA 1 (e.g. Rapid Vet-H Canine, DMS Laboratories) use whole blood and the test is completed within 2 minutes. Autoagglutination precludes the use of card tests for blood typing, as it may lead to erroneous results (i.e. a DEA 1-negative dog may be mistyped as DEA 1-positive). If in-saline autoagglutination is present, the cells should be washed to assess for persistence. If the RBC autoagglutination persists or the results of the typing are unclear, the recipient is considered to be DEA 1-negative until the autoagglutination resolves and an attempt can be made to type another blood sample. Weak positive results should be interpreted cautiously. If a weak positive result is obtained for a blood donor, it is safest to assume that the donor is DEA 1-positive. If a weak positive result is obtained for a recipient, it is safest to assume the recipient is DEA 1-negative.

An immunochromatographic cartridge test kit (e.g. DME VET DEA 1, Alvedia) is also available for in-house blood typing. The immunochromatographic strip contains two lines – a control line with lectin, which binds to any canine RBCs, and a test line with a monoclonal anti-DEA 1 antibody. The tip of the strip is placed into a RBC suspension (i.e. the test dog's RBCs in diluent) for approximately 2 minutes until the RBCs diffuse to the top of the strip. If there is no visible band at the control line, the result is invalid. The presence of a band at the DEA 1 line indicates the dog is DEA 1-positive. An advantage of the immunochromatographic cartridge over the card test is that RBC autoagglutination does not influence test results; therefore, dogs with immune-mediated haemolytic anaemia and persistent RBC agglutination can be accurately typed with this method. A study comparing various canine blood typing methods determined that the card test and immunochromatographic cartridge method were of comparable accuracy (90% and 93%, respectively), but the immunochromatographic method was 100% specific (i.e. there were no false positives), so there is no risk of mistakenly typing a patient as DEA 1-positive and transfusing type-mismatched RBCs (Seth *et al*., 2012).

Care should be taken when typing severely anaemic dogs. The prozone effect may prevent proper agglutination of RBCs from a DEA 1-positive dog with the DEA

reagent. Due to the low number of RBCs, the quantity of antigen is reduced relative to the amount of antibody present in the reagent, and consequently cross-linking between cells (agglutination reaction) may not occur. In this circumstance, it may be helpful to centrifuge the patient's whole blood test sample and remove one drop of the plasma to increase the relative concentration of RBCs. The RBCs and plasma are then remixed prior to performing the card test with the modified whole blood sample. Similarly, with the immunochromatographic cartridge method, the intensity of the test band for a DEA 1-positive dog may weaken with lowering PCV, while the control band appears unaffected (Seth *et al*., 2012). Finally, inaccurate results may occur if a patient has recently received a transfusion (prior to sampling for blood type determination).

Although it is advisable to determine the blood type of a dog prior to transfusion, in an emergency it may be necessary to assume that the patient is DEA 1-negative and use only a DEA 1-negative donor. Using donors of previously determined known blood types is then of the utmost importance. Patients should always be sampled prior to transfusion so blood typing can be performed at a later time.

Feline blood types

Blood groups in cats are described by the AB system, which includes three blood types: A, B and AB. The blood types A and B are inherited as a simple dominant trait, with A being dominant over B. Genotypically, type A cats are either homozygous a/a or heterozygous a/b, whereas type B cats are homozygous b/b. Type AB is a rare blood type in which there is a third allele recessive to the a allele and dominant to the b allele, leading to the expression of both A and B antigens.

Typing of cats prior to transfusion is imperative. Cats have naturally occurring alloantibodies to antigens not on their RBCs, with all B cats having strong anti-A antibodies and A cats having relatively weak anti-B antibodies; type AB cats do not have alloantibodies. RBC alloantibodies are found in a cat's plasma after 2–3 months of age. Given that sensitization to RBC antigens through transfusion or pregnancy is not necessary for alloantibody production, a cat may experience an acute and potentially life-threatening reaction to its first RBC transfusion if type-mismatched. Therefore, all donor and recipient cats must be blood typed prior to transfusion, even in an emergency. Type A cats must only receive type A blood and type B cats must only receive type B blood. The rarer AB cat should ideally receive type AB blood, but when that is not available type A blood is the next best choice.

The presence of naturally occurring alloantibodies may cause neonatal isoerythrolysis in type A and AB kittens born to a type B queen, due to the ingestion of colostral anti-A alloantibodies during the first 24 hours of life. Clinical signs of neonatal isoerythrolysis may develop within hours of colostrum ingestion, and include anaemia, haemoglobinaemia, jaundice and in some cases, death. Knowledge of the blood type of breeding cats and offspring, and removal and foster nursing of at-risk kittens for the first 24 hours of life, can prevent this transfer of colostral antibody and subsequent neonatal isoerythrolysis. Further information and advice is available from the International Cat Care website (www.icatcare.org).

Breeds with a documented higher prevalence of type B compared with the non-pedigree cat population include: British Shorthair, Cornish Rex, Devon Rex, Ragdoll, Turkish Van, Turkish Angora, Exotic Shorthair, Abyssinian, Himalayan, Birman, Burmese, Persian, Somali, Sphynx and Scottish Fold. Previous prevalence reports from the USA and UK suggest that the majority of domestic non-pedigree cats are type A (92.1–98.2%); however, recent studies indicate that the prevalence of type B is increasing. Overall, type AB is rare.

Another feline blood group antigen, *Mik*, separate from the AB system, was discovered as a result of cross-match testing incompatibility (Weinstein *et al*., 2007). Naturally occurring alloantibodies were found in plasma from blood donor cats which were *Mik*-antigen negative. Therefore, AB type compatibility does not ensure transfusion compatibility due to the possible presence of other RBC antigens and naturally occurring alloantibodies in the cat.

Blood typing for the AB system can be performed using several methods, including tube and slide agglutination assays, card test and immunochromatographic cartridge, with methods and potential issues similar to those described for canine blood typing. The simplest in-house blood typing methods available are an agglutination test card (RapidVet-H, DMS Laboratories) with a murine monocolonal anti-A antibody and *Triticum vulgaris* lectin as the B agglutinin, and immunochromatographic cartridges (DME VET A+B, Alvedia (Figure 14.1); RapidVet-H IC, DMS Laboratories), which contain monoclonal anti-A and anti-B antibodies. A study comparing these in-house kits with the standard tube method found good agreement for both the card test (91%) and the immunochromatographic cartridge (DME; 95%), with discordant results noted in a type A cat with FeLV-associated anaemia (Seth *et al*., 2011).

Occasionally, type AB cats may not be correctly identified with the card test, as only a weak agglutination reaction may occur in the A well. Although type AB cats are rare, this error could lead to misinterpretation of the type as B, with the potential for administration of a type-mismatched transfusion (type B blood to a type AB cat). When using in-clinic typing kits, it has been recommended to confirm AB or B typing results with either alloantibody (i.e. back-typing; Figure 14.2) or cross-match testing, or an alternative typing method at a commercial laboratory.



14.1 Feline blood typing using an immunochromatography cartridge (DME VET A+B, Alvedia, Lyon, France). The presence of a control (C) line indicates that results are valid; the presence of lines at A, B, and both A and B correspond to the blood type of each cat. (Courtesy of M Seth)

1. Submit EDTA blood sample from patient to a reference laboratory.
2. If in an emergency situation submitting a blood sample is not possible, perform back-typing (to screen for RBC alloantibodies by incubating plasma from recipient cat with washed 3–5% RBC suspension from a known type A cat) or a blood crossmatch (see Figure 14.4).

Back-typing (plasma from recipient cat)	Washed RBC suspension from type A donor
Recipient type AB	No agglutination
Recipient type B	3 to 4+ agglutination

Type AB recipient	Type A donor	Type B donor
Major crossmatch	Compatible	Compatible
Minor crossmatch	Compatible	3 to 4+ agglutination

Type B recipient	Type A donor	Type B donor
Major crossmatch	3 to 4+ agglutination	Compatible
Minor crossmatch	Compatible	Compatible

14.2 Confirmation of feline blood type AB or B determined by in-house typing kit.

Crossmatching

A blood crossmatch is performed to determine the serological compatibility between the patient and donor RBCs. Crossmatching should be performed whenever:

- The blood type of the feline recipient or donor is unknown
- The recipient (canine or feline) has been previously transfused more than 4 days ago
- There has been a less than expected increase in PCV post-transfusion (with no evidence of ongoing blood loss)
- There has been a history of a transfusion reaction
- The recipient's transfusion history is unknown.

In the event of the detection of the feline RBC antigen *Mik*, which is separate from the AB blood group system, and the presence of naturally occurring alloantibody to this novel RBC antigen that resulted in an acute haemolytic transfusion reaction, ideally a blood crossmatch should be performed for all cats, even before their first RBC transfusion. If it is not possible to obtain sufficient blood from an anaemic cat to perform a crossmatch, then an appropriately AB typed transfusion may be given, but the owners should be warned that there is a risk of an acute haemolytic transfusion reaction if the recipient has naturally occurring RBC alloantibodies.

A crossmatch allows detection of previous sensitization but does not prevent sensitization from occurring. Once the recipient receives a transfusion and 4–5 days have elapsed, a crossmatch must be repeated, as the recipient may no longer be compatible with the same donors (Figure 14.3).

The major crossmatch is an assessment of compatibility by agglutination between the donor RBCs and patient plasma/serum. The minor crossmatch assesses the interaction between the donor plasma/serum and patient RBCs. Minor crossmatch incompatibilities are less frequently the cause of haemolytic transfusion reactions and are mostly of concern when large volumes of plasma are to be administered. Patient autoagglutination or haemolysis may result in incompatibility, and a control should be run with the patient RBCs and patient serum (Figure 14.4). Some animals may have antibodies at too low a level to be detected by

Dogs

- Typing for DEA 1 status prior to a first transfusion is strongly recommended, with DEA 1-positive RBCs only being given to DEA 1-positive recipients
- If blood typing is not possible, then a first transfusion may be administered, with minimal risk of an acute, severe reaction
- A blood crossmatch is required for all patients that have received a RBC transfusion (even if given type-matched blood) more than 4 days previously

Cats

- Typing for AB status is mandatory in cats, even for a first transfusion, and type-matched blood must be used
- A blood crossmatch is strongly recommended prior to a first transfusion and essential if a patient has received a RBC transfusion more than 4 days previously

14.3 Key points for blood typing and crossmatching. DEA = dog erythrocyte antigen; RBC = red blood cell.

1. Collect blood into an EDTA tube from recipient and donor. Alternatively, for the donor sample, a segment of anticoagulated blood from the donor blood tubing may be used.
2. Centrifuge tubes to settle the RBCs; remove the supernatant and transfer to a clean, labelled glass or plastic tube.
3. Wash the RBCs three times with a normal saline suspension; discard the supernatant after each wash.
4. Resuspend the washed RBCs to create a 3–5% suspension by adding 0.2 ml of RBCs with 4.8 ml of normal saline (or 1 drop RBCs with 20 drops saline).
5. For each donor prepare three tubes labelled as major, minor and recipient control.
6. Add to each tube 1 drop of the appropriate 3–5% RBC suspension and 2 drops of plasma or serum according to the following:
   - Major crossmatch = donor RBCs + recipient plasma or serum
   - Minor crossmatch = recipient RBCs + donor plasma or serum
   - Recipient control = recipient RBCs + recipient plasma or serum.
7. Incubate the tubes for 15 minutes at 37°C (room temperature is usually sufficient).
8. Centrifuge the tubes for approximately 15 seconds to allow the RBCs to settle.
9. Examine the samples for haemolysis (reddening of the solution).
10. Gently tap the tubes to resuspend the RBCs; examine and score the tubes for agglutination as follows:
    - 4+ one solid aggregate of cells
    - 3+ several large clumps/aggregates of cells
    - 2+ medium-sized clumps/aggregates of cells, clear background
    - 1+ small/microscopic aggregates of cells, turbid reddish background
    - ± microscopic aggregates.
11. If macroscopic agglutination is not observed, transfer a small amount of the tube contents to a labelled glass slide and examine for microscopic agglutination (take care not to confuse with rouleaux formation).
12. Recipient control:
    - If there is no haemolysis or agglutination noted in the recipient control tube, the results are valid and incompatibilities can be interpreted
    - If there is haemolysis or agglutination present in equal scoring to the donor test samples, the compatibility and suitability of the donor cannot be accurately assessed.

Feline crossmatch abbreviated slide procedure

Given the presence of strong anti-A agglutinins in the plasma of type B cats, blood type incompatibilities can be detected in an abbreviated slide crossmatch procedure.

1. Follow crossmatch procedure steps 1–2 above.
2. For each donor prepare three slides labelled as major, minor and recipient control.
3. Place 1 drop of RBCs and 2 drops of plasma or serum on to each slide according to the following:
   - Major crossmatch = donor RBCs + recipient plasma or serum
   - Minor crossmatch = recipient RBCs + donor plasma or serum
   - Recipient control = recipient RBCs + recipient plasma or serum.
4. Gently rock the slides to mix the plasma/serum and RBCs and examine for haemagglutination after 15 minutes (presence of agglutination is indicative of incompatibility); recipient agglutination will invalidate results.

14.4 Blood crossmatch procedure.

crossmatch and may then experience a mild haemolytic reaction despite an apparently compatible result.

Despite using blood products from a crossmatch-compatible donor, it is still possible for a patient to experience a haemolytic or non-haemolytic transfusion reaction, and recipient monitoring during and after administration of blood products is essential.

Collection, processing and storage of blood

Blood collection systems

All whole blood collection should take place in an aseptic manner and using an appropriate anticoagulant. The anticoagulant–preservative solutions most often used are ACD (acid-citrate-dextrose), CPD (citrate-phosphate-dextrose) or CPDA-1 (citrate-phosphate-dextrose-adenine). Most of the commercially available blood collection systems contain either CPD or CPDA-1. The volume of anticoagulant used and the duration of time for which the blood product can be stored vary depending on the anticoagulant–preservative solution and the collection method. ACD is used at a ratio of 1 ml of anticoagulant to 7–9 ml of blood, and CPD and CPDA-1 are typically used in a ratio of 1 ml anticoagulant to 7 ml of blood. Sodium citrate alone (without RBC preservatives) may be used at a ratio of 1 ml anticoagulant to 9 ml of blood if blood is to be stored <24 hours prior to administration. Use of heparin is not recommended.

Whole blood may be collected using a closed (preferred) or open collection system. A closed system is one in which the only exposure of the collection bag or its contents to air prior to administration is when the needle is uncapped to perform venepuncture during collection. Examples of a closed system are commercially available 450 ml blood collection bags containing 63 ml of CPD or CPDA-1 anticoagulant with an attached 16 G needle. These are most commonly used in dogs weighing >23 kg. Multi-bag systems with empty transfer satellite bags and nutrient additive solution may be used for component processing (Figure 14.5).

Any system in which there is one or more additional sites of potential bacterial contamination during blood collection or processing is by definition an open system.



14.5 Example of a commercially available closed collection system with multiple connecting bags allowing processing of whole blood and storage as packed red blood cells and plasma.

All blood products collected in an open system must be administered within 4 hours, or if stored in a refrigerator (1–6°C) they must be used within 24 hours. Blood collection using syringes or empty bags with added anticoagulant, as frequently used for cats and other small volume collections, is classified as an open system. However, a feline closed collection system (Figure 14.6) has been prepared by the Penn Animal Blood Bank by the sterile docking of an 18 G apheresis needle (SysLoc Safety A.V. Fistula Needle Set, JMS, Singapore) to a 75 ml paediatric transfer pack containing anticoagulant–preservative solution, using a sterile tubing welder (Terumo, Somerset, NJ).

The volume of blood that may be collected safely from canine and feline donors is approximately 20% of their blood volume, every 4 weeks. A recommended volume limit is 18 ml/kg for dogs and 11 ml/kg for cats based on lean bodyweight. Most volunteer donor schemes using client-owned pets as donors extend the donation interval to every 8–12 weeks. A study evaluating the effect of repeated blood donations on iron status of canine blood donors revealed that dogs donating 11.4 ml/kg every 2 months maintained haematological variables (assessed 10 days post-donation) within reference range but had a significant decrease in iron stores (serum ferritin concentration) at the end of 1 year, suggesting that iron-related variables should be monitored in dogs donating blood frequently (<2 months) for a prolonged period of time (Ferreira *et al.*, 2014).



14.6 Example of a feline (or small-volume) closed collection system. An 18 G apheresis needle has been sterilely docked to a 75 ml pediatric transfer pack containing citrate-phosphate-dextrose-adenine.

Donor health check

Prior to every donation, information on the donor animal is reviewed and a brief questionnaire is completed by the owner. The age and general good health of the donor and date of last donation are confirmed. Many aspects will have been covered through the donor's selection procedure; however, it is important to assess any changes in status for a repeat donor. A full physical examination is performed and noted in the donor's file. A small sample of blood for measurement of PCV or Hb level is obtained prior to every donation to ensure the donor has a normal RBC mass. For a canine donors the PCV should be >40% (Hb >130 g/l), and for a feline donor the PCV should be >30% (Hb >100 g/l) and ideally PCV >35%. The result is recorded in the donor's file. This also allows for recognition of trends in the donor animal's PCV over time.

Blood collection

The jugular vein is the recommended venepuncture site in both dogs and cats because of its size and accessibility. Collection should be initiated with a single, smooth needle stick to avoid cell damage or excessive activation of coagulation factors. Strict aseptic technique minimizes the possibility of bacterial contamination. All donors must be closely monitored during blood collection by assessing their mucous membrane colour, pulse rate and quality, and respiratory rate and effort. If any concerns develop, the donation should be discontinued.

Most dogs are able to donate without the use of sedation, and it is preferable to train a donor to the procedure. Placing the dog in lateral recumbency, on a soft blanket on a table, facilitates comfortable restraint (for donor and veterinary personnel) for the approximately 10 minutes required for blood collection (Figure 14.7). This position also allows adequate digital pressure to be applied to the venepuncture site for haemostasis whilst the animal maintains a recumbent position following donation. Other positions, in decreasing order of authors' preference, include sitting, standing and sternal recumbency.

Collection of whole blood from dogs using a commercial blood bag may be accomplished via gravity alone (Figure 14.8); however, use of a specialized vacuum chamber may decrease the donation time and therefore the amount of time the donor must be restrained (Figure 14.9). A cylindrical acrylic plastic chamber houses the collection bag during the donation, with the tubing to the donor passing out through a notch at the top of the chamber. A vacuum source that can be regulated at low vacuum pressures (<127 mm Hg; <17 kPa) is attached to the chamber, and the entire chamber, with collection bag inserted, is placed on a gram scale (Figure 14.10). The gram scale is used to monitor the weight of the bag during collection, ensuring that an adequate and not excessive amount of blood is collected to preserve the appropriate anticoagulant to blood ratio. When collecting blood via gravity alone, the bag should be placed on the scale and the weight of the bag and anticoagulant measured prior to venepuncture. Again, the bag should be weighed during donation to confirm collection of the correct blood volume. The volume of blood that should be collected into a commercial blood bag is 450 ml, with an allowable 10% variance (405–495 ml). The weight of 1 ml of canine blood is approximately 1.053 g; therefore, the weight of an acceptable unit using one of these bags is approximately 426–521 g.



14.7 Blood donation with the donor dog in lateral recumbency, using a closed collection system.

1. Clip hair over the jugular groove and apply EMLA cream (lidocaine 2.5% and prilocaine 2.5%). This is usually performed at the time of the health check, prior to the donor being placed on the donation table. (Note: The use of a topical anaesthetic cream is optional.)
2. Restrain the animal securely and comfortably (lateral recumbency on a table is recommended).
3. Prepare the area aseptically.
4. Apply pressure at the thoracic inlet to raise the jugular vein and facilitate palpation and visualization of the vessel. Avoid contamination of the venepuncture site.
5. Use a guarded haemostat or the clamp provided with the blood collection bag on the donor tubing to prevent air from entering the bag when the needle is exposed.
6. Remove the needle cap and perform venepuncture using the 16 G needle attached to the collection bag. Remove the clamp or the haemostat. If no flash of blood is seen in the tubing, check the needle placement and check for any occlusion in the tubing. The needle may be repositioned; however, it should not be fully withdrawn from the donor. If the needle is withdrawn, the line must once again be clamped to prevent entry of air into the bag.
7. The bag should be positioned lower than the donor to aid in gravitational flow. Suction may assist in collection by use of an appropriately designed vacuum chamber (see Figures 14.9 and 14.10).
8. Periodically invert the bag gently to mix blood and anticoagulant.
9. When the bag is full (405–495 ml blood = 426–521 g), clamp the collection tubing, remove the needle from the jugular vein, and apply pressure to the venepuncture site to prevent haematoma formation.
10. Remove the clamp from the collection tubing, and, using a tube stripper, strip the blood from the tubing to allow the blood to be mixed with anticoagulant in the collection bag prior to preparing crossmatch segments.
11. After mixing the blood in the collection bag by inverting the bag several times, allow the tubing to refill with anticoagulated blood and clamp the distal (needle) end with a hand sealer clip or heat sealer. If these are not available a tight knot may be tied in the line.
12. Clamp the entire length of tubing in 10 cm segments to be used for subsequent crossmatches.
13. Label the bag with donor identification, date of collection, date of expiration and donor blood type.

If using a multiple bag system for blood component preparation, the bag is now ready for the processing procedure (centrifugation, plasma extraction).

14.8 Procedure for canine whole blood collection.

1. Place the vacuum chamber on the gram scale.
2. Place the collection bag in the chamber, hanging the bag from the clip on the chamber lid.
3. Exit the donor tubing by placing it in the notch on the top of the chamber. Ensure that enough tubing length remains within the cylinder to prevent occlusion (tight kinking of the line) during collection.
4. Place the lid on the chamber and turn the suction on to a low level (50 mm Hg; 7 kPa). Try to gently lift the chamber by the lid to ensure an adequate vacuum seal. If the seal is not tight, or if a whistling noise is heard, place a small piece of moistened cotton at the notch where the tubing exits the chamber.
5. The suction machine must be turned off before venepuncture is performed on the donor. Follow steps 1–6 listed in the procedure for canine whole blood collection (see Figure 14.8).
6. Once a flashback is obtained in the donor tubing line, turn on the suction machine. The recommended vacuum pressure is 127 mm Hg (17 kPa). Gentle mixing of the blood and anticoagulant during collection is less necessary during vacuum assisted collection than gravity flow collection. However, if the chamber must be entered during the collection (slowing or cessation of blood flow, checking tube for occlusion) suction must be discontinued while adjustments are being made.
7. When the bag is full (405–495 ml blood = 426–521 g), turn off the suction, clamp the donor tubing, remove the needle from the jugular vein and apply pressure to the venepuncture site to prevent haematoma formation.
8. Follow steps 10–13 listed in the procedure for canine whole blood collection (see Figure 14.8).

14.9 Procedure for vacuum-assisted canine blood collection.



14.10 Vacuum chamber with an empty collection bag in place. Suction is applied to the chamber, facilitating rapid blood collection. The entire apparatus is placed on a scale during donation so that the volume of blood collected can be monitored.

Cats typically require sedation. It is suggested that each practice develop, a protocol with which they are comfortable and that works with their donor animals. Examples include combinations of ketamine and midazolam intravenously or isoflurane/oxygen anaesthesia by mask (Figure 14.11). A suggested procedure for collection of feline blood using an open collection system is described in Figure 14.12. Alternatively, if a closed feline collection system is used, the bag containing the anticoagulant–preservative solution may be suspended in the same chamber as used for canine collections, but with the blood collected by gravity alone; vacuum-assisted collection is not recommended, as it may cause the jugular vein of a cat to collapse, impeding blood flow.

- Butorphanol at 0.1–0.2 mg/kg ± diazepam at 0.5 mg/kg i.v. (same syringe)
- Ketamine at 2 mg/kg and midazolam at 0.1 mg/kg i.v. (same syringe), additional boluses of a quarter to half the original dose as needed
- Ketamine at 5–10 mg/kg and midazolam at 0.2 mg/kg i.m. (same syringe), with additional boluses of ketamine at 1 mg/kg i.v. as needed
- Mask isoflurane/oxygen anaesthesia

14.11 Examples of feline donor sedation protocols.

An 18 G needle, 19 G butterfly catheter or 18 G over-the-needle intravenous catheter is required for dogs; typically a 19 or 21 G butterfly catheter is used for cats. Syringes for collection should be pre-filled with an appropriate anticoagulant (1 ml CPDA-1 per 7 ml blood).

1. Cats typically require sedation. An intravenous catheter may be placed in the cephalic vein of the feline donor, either before (preferable) or after sedation for the purpose of administering intravenous fluids after the blood donation (optional).
2. Steps 1–4 are performed as in the canine whole blood collection method (see Figure 14.8). The feline donor is restrained in sternal recumbency, with the forelimbs over the edge of a table and the head raised.
3. Perform venepuncture. Without removing the needle, fill each syringe in turn. The syringe can be gently rocked to ensure mixing of blood and anticoagulant during collection. If an over-the-needle catheter is used, remove the stylet following the venepuncture and advance the catheter into the vein. Attach an extension set, and fill each syringe in turn.
4. Invert the syringes gently several times after collection to mix blood and anticoagulant.
5. After collection, remove the needle from the jugular vein and apply pressure to the venepuncture site to prevent haematoma formation.

14.12 Procedure for the syringe method of collection. This is most commonly used for collection of feline blood or small volumes of canine blood or when a closed collection system is not available.

Following donation, food and water are offered to canine donors. Activity should be restricted to lead walks only for the next 24 hours, and it is advised that a harness or lead passed under the chest is used instead of a neck collar and lead, to avoid pressure on the jugular venepuncture site. The recommended aftercare of blood donor cats varies, as some blood banks routinely administer intravenous crystalloid solution (30 ml/kg over 3 hours), while others do not provide any replacement fluids. The donor must be closely observed during recovery from sedation/anaesthesia and may be offered food and water once fully awake.

Blood components: processing, storage and indications

In larger veterinary centres with a high emergency and critical care caseload, preparation of blood components becomes essential to extend resources and to ensure products are available when they are needed regardless of the time of day or night. In addition, the use of blood components permits specific replacement therapy and reduces the number of transfusion reactions. Blood component processing requires variable-speed, temperature-controlled centrifuges. The precise separation protocol used is dependent on the centrifuge and blood components being prepared. To prevent microbial contamination a closed collection system must be used, and the transfer of components to satellite bags must be contained within the system by integral tubing. The tubing should be sealed prior to unit storage using either a hand-held clip sealer or heat sealer. If blood is collected into an open system it should be refrigerated and administered within 24 hours, in which case the use of blood component therapy is less applicable.

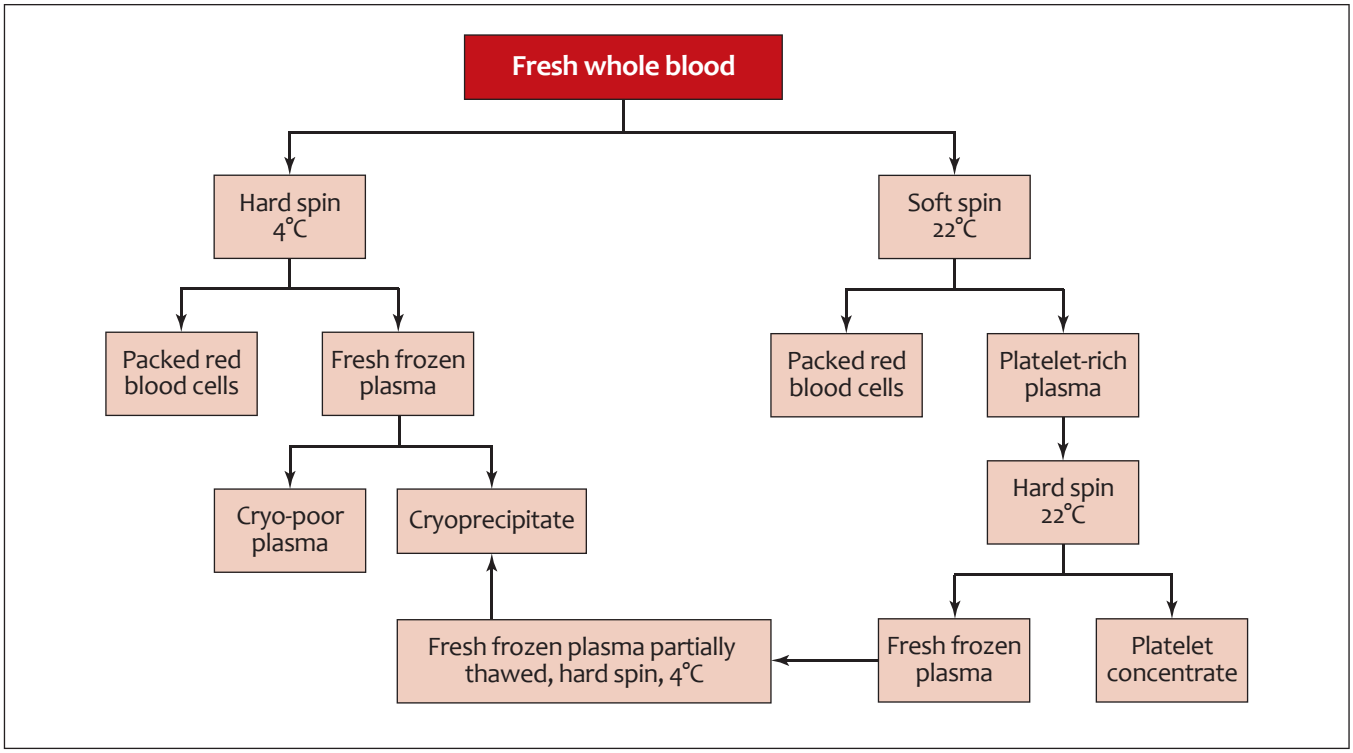
All blood products should be labelled with product type, donor identification, donor blood type, date of collection and date of expiration.

Fresh whole blood and stored whole blood

Initial blood collection yields fresh whole blood (FWB), which by definition is not refrigerated and is used within 8 hours of collection. All blood components (RBCs, platelets, labile and stable coagulation factors, plasma proteins) are present and functional. FWB is the product most commonly used in smaller private veterinary practices; however, if blood components are available, the administration of FWB should be restricted to those anaemic patients with concurrent haemostatic defects. FWB not used within 8 hours of collection may be stored in a refrigerator at 1–6°C for approximately 21 or 28 days when collected in CPD or CPDA-1, respectively. The unit is then classified as stored whole blood (SWB), which differs from FWB only by the absence of functional labile clotting factors and platelets. When available, SWB may be useful in anaemic animals with concurrent hypoproteinaemia; however, in such cases, PRBCs and plasma or a synthetic colloid may also be an effective treatment option.

Packed red blood cells

FWB can be separated into PRBCs, fresh plasma and platelet concentrates (Figure 14.13). PRBCs are separated from the plasma by centrifugation at 5000 g for 5 minutes at 4°C. The PCV of the PRBCs is usually in the range of 70–80%, with the volume yield dependent on the donor haematocrit. Use of a nutrient additive solution, such as



14.13 Blood component processing.

Adsol (100 ml volume added to PRBCs from a full donation of 450 (± 10%) ml whole blood; the volume of Adsol can be adjusted for smaller donations), will typically lower the PCV of the PRBCs to 55–65%. Various additive solutions are composed of saline, adenine, and dextrose ± mannitol ± citrate/citric acid, and are intended to extend the shelf-life of stored PRBCs.

PRBCs (as well as SWB) should be stored in a refrigerator maintained at 1–6°C, with the bag in an upright position. Positioning the bag in this manner maximizes gas exchange with the RBC suspension to help preserve the viability of the RBCs during storage and following transfusion. The shelf-life of PRBCs is similar to SWB but in the presence of an additive solution is extended to 35–37 days (Wardrop *et al*., 1994), though some blood banks extend storage of canine PRBCs in various additive solutions to 42 days.

There is growing concern in human medicine that transfusion of 'older' PRBCs (generally defined as >14 days of storage) is associated with increased mortality, multiple organ dysfunction and/or sepsis in certain populations of critically ill patients (Wang *et al*., 2012). The mechanisms by which transfusions of older, stored RBCs may increase morbidity and mortality are not yet known, but proposed mediators include microparticles that accumulate in PRBC unit during storage, cell-free Hb released following transfusion, and non-transferrin-bound iron that increases in the circulation due to rapid removal of older, stored RBCs by macrophages (Hod *et al*., 2010; Kim-Shapiro *et al*., 2011). In a prospective, controlled, crossover study of healthy dogs randomized to receive autologous PRBC transfusions (pre-storage leucoreduced or non-leucoreduced) stored for 7 days (fresh) and 28 days (old), administration of 28-day-old PRBCs induced a proinflammatory cytokine response exemplified by an increase in monocyte chemoattractant protein-1 and accompanied by increased neutrophil counts and decreased platelet counts (Callan *et al*., 2013). There was no difference in inflammatory response between dogs receiving pre-storage leucoreduced and non-leucoreduced PRBCs, indicating that this response was not mediated by white blood cells or platelets (also removed by leucoreduction) in the stored PRBCs. Furthermore, there was evidence of extravascular haemolysis and a substantial increase in non-transferrin-bound iron after administration of PRBCs (with Adsol) stored for 28 days, raising the question of whether even 28 day storage is appropriate for PRBCs used in critically ill dogs.

Specialized blood storage refrigerators with built-in temperature alarms are available, or a dedicated regular household refrigerator with low in-and-out traffic may be used. A refrigerator thermometer should be checked daily to ensure appropriate storage conditions. A recent publication highlights the importance of appropriate RBC storage, as acute life-threatening transfusion reactions in four dogs (two of which died, and one was euthanased) were attributed to administration of PRBCs that were lysed *in vitro* as a result of temperature fluctuations in a multi-use refrigerator in a clinical practice (Patterson *et al*., 2011).

PRBC transfusion is indicated in animals in need of additional oxygen-carrying support due to haemorrhage, haemolysis or ineffective erythropoiesis (see Chapter 13).

Fresh frozen plasma and frozen plasma

Fresh frozen plasma (FFP) is plasma separated from whole blood and frozen within 24 hours of collection, in accordance with the standard of the United Kingdom National Health Service Blood and Transplant (NHSBT). Previously, there was a limit of 8 hours for processing of whole blood to harvest plasma as FFP. However, a study evaluating the coagulation factor and haemostatic protein content of canine plasma after storage of whole blood at ambient temperature for 8, 12 and 24 hours indicated that delaying processing until 24 hours did not adversely affect the quality of the FFP (Walton *et al*., 2014). FFP has a shelf-life

of 12 months when stored at or below –18°C. FFP provides all of the haemostatic proteins, albumin and globulin. FFP units stored for longer than 1 year may be relabelled as frozen plasma (FP) and stored for up to 5 years from collection. The haemostatic proteins in FP retain variable activity, with significantly reduced levels of the labile coagulation factors V and VIII. Therefore, FP may be used primarily as a source of albumin and globulin; it is not an appropriate plasma product for management of coagulopathies.

In clinical practice, unforeseen circumstances may result in a thawed unit of FFP not being administered to the intended recipient. In such a case, a closed unit of FFP (canine or feline) may be refrigerated and refrozen within 1 hour of initial thawing without a deleterious effect on the haemostatic protein activity or content of the unit (Yaxley *et al*., 2010). In this study comparing the stability of haemostatic proteins in freeze-thawed-cycled FFP with FFP that remained frozen until analysis, the thawed plasma was stored at 4°C before refreezing, so it is unclear if storage at room temperature for 1 hour or refrigerated storage duration of longer than 1 hour before refreezing would have a deleterious effect on coagulation factor stability.

Regular household freezers may suffice for storage of plasma products, but the temperature may vary depending on the section of the freezer used. The temperature should be checked daily using a thermometer, and opening and closing of the freezer should be minimized. When initially freezing the plasma, an elastic band should be placed around the bag, which is removed once frozen. This creates a 'waist' in the bag (Figure 14.14). Disappearance of this waist during storage would suggest that the unit has thawed and refrozen, signifying compromise of storage conditions and potentially plasma quality. The entire plasma bag should be enclosed in a sealed plastic bag, in which it should remain during plasma thawing to protect the injection ports from contamination. The frozen plasma unit is vulnerable to cracking if dropped, and should be handled with care. Individual unit cardboard storage boxes are available to provide additional protection during storage of plasma products.



14.14 A unit of fresh frozen plasma showing the 'waist' created by freezing with a rubber band in place.

FFP is indicated for use in animals with bleeding due to inherited or acquired coagulopathies (e.g. haemophilia, vitamin K deficiency, disseminated intravascular coagulation (DIC), liver failure, *Angiostrongylus vasorum* infection), and may be used prophylactically in surgical patients with known coagulopathies. As FFP and FP contain plasma proteins (albumin and globulin), either may be used in animals with hypoproteinaemia; however, large volumes and repeated transfusions are required to produce a clinically significant and sustained improvement in plasma protein.

Platelet-rich plasma and platelet concentrate

Platelet-rich plasma (PRP) and platelet concentrate (PC) may be prepared from FWB; however, these products are some of the most challenging to prepare due to the delicate nature of platelets. To enhance survival and function of the platelets in the resulting product, extreme care and attention must be given to the unit during all phases of handling. Some leucocyte reduction filters (present in many commercially available blood bags in the UK) will also remove platelets, thus blood collected for production of platelet products must use a collection bag without the in-line pre-storage leucocyte reduction filter. FWB is centrifuged on a 'soft' spin, the actual speed and time of which are dependent on the particular centrifuge, with the aim of producing a platelet unit containing at least 5 x 10^{10} platelets. An example of a separation protocol is 2000 g for 3 minutes at 20–24°C (i.e. a lower centrifugation speed and time compared with the preparation of PRBCs and FFP, and the product is not refrigerated), with the brake on the centrifuge turned to a low setting or off to minimize RBC contamination in the supernatant (PRP) since the RBCs are less tightly packed following soft spin centrifugation. The PRP is separated from the PRBCs and may either be administered to the recipient, stored (see below) or further processed into PC and FFP. To prepare PC, PRP with an attached empty satellite bag is centrifuged at 5000 g for 5 minutes at 20–24°C. All but approximately 35–70 ml of the supernatant plasma is transferred into the empty bag and frozen (FFP), leaving the PC in a small volume of plasma in the second bag. PRP and PC may be stored at 20–24°C, with continuous gentle agitation, for 5 days when collected using a closed system. As they are stored at room temperature, platelet products are susceptible to bacterial proliferation, and if collected in an open system, they should be used within 4 hours of collection. These products are used when there is severe, uncontrollable or life-threatening bleeding (e.g. pulmonary haemorrhage) caused by thrombocytopenia or thrombopathia, although the difficulties associated with their preparation often result in the use of more readily available FWB instead.

Cryoprecipitate (Cryo) is a plasma component that is prepared by freeze-thaw precipitation of proteins, yielding a source of concentrated von Willebrand factor, factor VIII, factor XIII, fibrinogen and fibronectin from a unit of FFP. Cryo can be prepared from FFP within 12 months of collection. A unit of FFP is slowly thawed in a refrigerator at 1–6°C until it is of a slushy consistency or until only approximately 10% of the plasma remains frozen, and then centrifuged at 5000 g for 5 minutes at 4°C. The cryo-poor plasma (CPP or the cryosupernatant) is expressed into a satellite bag, leaving behind the Cryo in a small volume of plasma (20–25 ml). The CPP contains many clotting factors (including vitamin K-dependent factors II, VII, IX and X), as well as other anticoagulant and fibrinolytic factors, albumin and globulin. The Cryo and CPP are

immediately refrozen at or below –18°C and should be used within 1 year of original collection. Cryo is used in the management of patients with bleeding due to deficiency or dysfunction of factor VIII (haemophilia A), von Willebrand factor or fibrinogen. CPP may be used for treatment of all other hereditary coagulopathies and vitamin K deficiency, as well as hypoproteinaemia.

Haemoglobin-based oxygen carriers

Haemoglobin based oxygen carriers have been an area of active research for many years. They have the theoretical benefit of increasing the oxygen carrying capacity of the blood without any of the risks associated with transfusing cells. One product Oxyglobin® has been licensed for use in animals although it is not currently on the market. Some further information on Oxyglobin® is included here in case it or other similar products become available again.

Oxyglobin® is a sterile solution of purified, polymerized bovine haemoglobin that increases plasma haemoglobin concentration, shifting the majority of the oxygen content of the blood to the plasma. It has been approved for use in dogs for the treatment of anaemia, regardless of cause. Although Oxyglobin® has been used in cats to provide oxygen-carrying support in cases of anaemia (Gibson *et al*., 2002), it is not licensed for use in this species. Oxyglobin® should be administered with care. Given that it is a very effective colloid, which causes significant intravascular volume expansion, patients receiving Oxyglobin® should be monitored for evidence of circulatory overload and possible development of pulmonary oedema and/or pleural effusion. Plasma Hb concentrations of patients who have received Oxyglobin® should be monitored using a haemoglobinometer (e.g. HemoCue AB, Sweden).

Blood product selection

Blood products are used to treat a variety of conditions, including those associated with anaemia (haemorrhage, haemolysis or ineffective erythropoiesis), coagulopathies, sepsis, disseminated intravascular coagulation and specific factor deficiencies.

RBC products provide the recipient with additional red cell mass to increase the oxygen-carrying capacity of the blood, and thus improve oxygen delivery to the tissues. There is not a precise PCV below which a transfusion is required, although any patient with a PCV <20% should be considered a potential candidate, and almost all patients would benefit once the PCV is ≤12%. In some animals with peracute blood loss and hypovolaemia, RBC transfusions may be administered even though their PCV may be normal. These patients will predictably develop a low PCV following fluid resuscitation with asanguineous fluids. The decision to transfuse RBCs is therefore based on several factors, including the Hb concentration (or PCV), onset of anaemia (acute *versus* chronic), presence of ongoing losses and, most importantly, the clinical signs of the patient. Tachycardia, bounding peripheral pulses, collapse, lethargy and weakness are all signs that should prompt consideration of a RBC transfusion.

Plasma products are a source of coagulation factors and various plasma proteins, and deficiencies of these factors or selected proteins are indications for their use. The benefit of plasma transfusion to a hypoproteinaemic patient, however, is limited, as large volumes of plasma would be required to correct the albumin deficit. Other modes of therapy (nutritional support, use of colloids) are suggested for this condition.

Blood product administration

Blood products are usually administered intravenously, but may also be given via the intraosseous route if venous access cannot be obtained (e.g. kittens, puppies). An in-line blood filter (170–260 μm) is required for all blood products (including plasma) and is incorporated in standard blood infusion sets. A neonatal/paediatric syringe set with 150 μm filter (Charter Medical, Winston-Salem, NC, USA; Figure 14.15) is useful for administering smaller volumes of blood products and may be preferable to the 18 μm microaggregate filter (e.g. Hemo-Nate) for administration of RBC products to minimize the risk of *in vitro* haemolysis due to small pore size. Stored RBC products do not need to be warmed prior to use, unless they are being given to neonates or very small animals. Plasma products are gently thawed in a warm water bath prior to administration. PRBCs stored without an additive solution may be resuspended in or co-administered with 100 ml physiological saline to decrease their viscosity.



14.15 A neonatal syringe set with 150 μm filter used for administration of small volumes of red blood cells.

The amount of blood product to be administered depends on the specific product, desired effect and patient's response. A general rule of thumb is that 2 ml of transfused whole blood/kg recipient bodyweight will raise the PCV by 1%. Most patients will receive between 10 and 22 ml/kg, and a suggested formula to calculate the volume of whole blood required for transfusion is:

Volume (ml) = 85 (dog) or 60 (cat) x bodyweight (kg) x [(desired PCV – actual PCV)/donor PCV]

However, this does not take into consideration concurrent ongoing blood losses or fluid therapy in critical patients, therefore it is essential to measure the patient's PCV following transfusion in order to determine the response. For PRBCs or FFP, the average volume for infusion is 10–15 ml/kg or 6–12 ml/kg, respectively.

The rate of administration depends on the cardiovascular status of the recipient. In general, the rate should only be 0.25–1.0 ml/kg/h for the first 20 minutes. If the transfusion is well tolerated, the rate may then be increased to deliver the remaining product within 2–4 hours. In an animal with an increased risk of volume overload (cardiovascular disease, impaired renal function) the rate of administration should not exceed 2–3 ml/kg/h. If it is likely to take more than 4 hours to deliver the desired volume, the product may be divided so that a portion remains refrigerated for later use.

Animals should not receive food or medication during a transfusion, and the only fluid that may be administered through the same catheter is 0.9% saline.

Visual inspection of the product is necessary, especially when using stored RBCs or plasma. Discoloration of the RBCs (brown, purple) or the suspension fluid, or the presence of clots, may indicate bacterial contamination, haemolysis or other storage lesions. Plasma bags must be examined for evidence of thawing and refreezing, or cracking and tearing of the bag.

Monitoring transfusions

The following parameters should be measured prior to (baseline), every 15–30 minutes during, and 1, 12 and 24 hours after transfusion:

- Attitude
- Rectal temperature
- Pulse rate and quality
- Respiratory rate and character
- Mucous membrane colour and capillary refill time
- Urine colour (when available).

The PCV/total protein and plasma colour (to assess for the development of haemolysis) should be monitored prior to, upon completion, and at 12 and 24 hours after transfusion.

It is helpful to design a transfusion monitoring sheet, with time points and monitoring parameters noted, to encourage diligent recording during and after the transfusion. Careful monitoring will allow for prompt recognition and treatment of transfusion reactions as well as evaluation of transfusion efficacy.

Adverse reactions

Any undesired side effect noted as a consequence of a blood product transfusion is considered a transfusion reaction. The reported frequency of transfusion reactions is variable, as is their severity. Transfusion reactions may be classified as immunological (haemolytic or non-haemolytic) and non-immunological, as well as acute or delayed.

Preventative measures necessary to minimize the risk of transfusion reactions include appropriate donor screening and appropriate collection, preparation, storage and administration of products. Adherence to standard protocols helps to ensure the safety and efficacy of transfusions in practice.

Immunological transfusion reactions

The most concerning type of transfusion reaction is an acute haemolytic reaction with intravascular haemolysis, which is an antigen–antibody, type II hypersensitivity reaction. This type of reaction is seen in type B cats receiving type A blood, DEA 1-negative dogs sensitized to DEA 1 upon repeated exposure, and potentially other sensitized patients with alloantibody-mediated RBC incompatibilities. Clinical signs may include fever, tachycardia, dyspnoea, muscle tremors, vomiting, weakness, collapse, haemoglobinaemia, and haemoglobinuria. These reactions may lead to shock, DIC and, potentially, death.

If an acute haemolytic transfusion reaction is suspected, the transfusion should be discontinued immediately and fluid therapy initiated for treatment of the clinical signs of shock. Antihistamines and corticosteroids may be administered. Aggressive fluid therapy may be required if the patient becomes hypotensive, thus patients should be carefully monitored for development of fluid overload (measurement of central venous pressure, heart rate, lung auscultation). Blood pressure and urine output should be monitored, as hypotension and oliguria may ensue.

Febrile non-haemolytic transfusion reactions and reactions to blood that has been contaminated with bacteria may have similar signs, with development of a significant fever during or shortly after starting the transfusion. The donor and recipient blood type should be confirmed and a crossmatch performed. The product type, date of expiration, volume and rate of administration should be confirmed. A sample of donor and recipient blood should be examined for evidence of haemolysis and saved for microbial culture and further infectious disease screening, if needed. A Gram stain of donor blood may be helpful initially to investigate possible unit contamination, and, if bacterial contamination is suspected, broad-spectrum intravenous antibiotic therapy should be initiated. As DIC and renal failure may occur, monitoring the animal's coagulation profile, urine output, blood urea nitrogen, creatinine and electrolytes is advisable.

A delayed haemolytic reaction with extravascular haemolysis may be recognized 2–21 days post-transfusion, with similar, although less severe, signs compared with an acute haemolytic reaction (± bilirubinaemia/bilirubinuria). The owner may notice jaundice or anorexia, and on examination the animal may be febrile. However, a delayed haemolytic transfusion reaction may go unnoticed and only be considered when the clinician notes an unexpected decline in PCV. A blood crossmatch between the recipient and the same donor, using plasma from the recipient at the time of the suspected delayed haemolytic transfusion reaction, could be performed to document development of RBC incompatibility post-transfusion.

Non-haemolytic immunological reactions are acute type I hypersensitivity reactions (allergic or anaphylactic), most often mediated by IgE and mast cells. They have a range of clinical signs including urticaria, pruritus, erythema, oedema, vomiting and dyspnoea secondary to pulmonary oedema. If this type of reaction occurs, the transfusion should be discontinued and the patient examined for evidence of haemolysis and shock. Corticosteroids (dexamethasone 0.5–1.0 mg/kg i.v.) and antihistamines may be required. Suggested antihistamine dosages are as follows:

- Diphenhydramine: 1 mg/kg i.m. q12h in dogs and cats
- Chlorpheniramine: maximum recommended dose 0.5 mg/kg q12h in both dogs and cats:
  - Dogs: small to medium-sized, 2.5–5 mg i.m.
  - Dogs: medium to large, 5–10 mg i.m.
  - Cats: 2–4 mg/cat orally q12h.

If the reaction subsides, the transfusion may be restarted at 25–50% of the previous rate. If there is evidence of an anaphylactic or anaphylactoid reaction, treatment for shock (e.g. fluid therapy, adrenaline) should be instituted. The transfusion should not be restarted in the case of such a severe adverse reaction.

Reactions to leucocytes and platelets may occur, manifested by a febrile non-haemolytic transfusion reaction, which may last up to 20 hours post-transfusion. These are recognized as an increase in body temperature of >1°C without an obvious underlying cause. The risk of these types of reaction may be minimized by the use of pre-storage leucocyte reduction filters in the preparation of blood components.

Non-immunological transfusion reactions

Many non-immunological transfusion reactions have been described. Anaphylactoid reactions, which often result from too rapid an infusion rate, may be seen and tend to

subside after discontinuation of the transfusion or reduction of the infusion rate. Circulatory overload may occur in any patient receiving excessive volumes of blood products, or those with cardiac or renal disease; treatment with diuretics may be required. Hypocalcaemia is identified most commonly following administration of large volumes or plasma or whole blood, and is a result of citrate intoxication. Patients with impaired liver function are at greatest risk. Clinical signs of hypocalcaemia may be noted (vomiting, muscle tremors, tetany, electrocardiogram changes), and treatment includes supplementation with calcium gluconate or calcium chloride.

Other recognized non-immunological reactions include hypothermia, coagulopathy, microbial contamination and infectious disease transmission. The importance of careful screening of blood donors and meticulous collection, processing and storage of blood components cannot be overstated, as fatal non-immunological transfusion reactions have been reported in veterinary patients receiving bacterially contaminated blood units and RBC products with in vitro haemolysis due to improper storage conditions.

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Chapter 15

Reproductive and paediatric emergencies

Erica Reineke and Dan Lewis

Reproductive emergencies are a common presentation in small animal practice. While many of these involve peri-parturient problems, diseases of the reproductive tract are frequently encountered in males and non-pregnant females and often carry a favourable prognosis if treated appropriately. Unfortunately, neonatal disease often carries a much poorer prognosis due to several factors. Nevertheless, timely veterinary intervention coupled with knowledge of the differing physiological requirements of neonatal puppies and kittens is often all that is required to ensure survival.

Reproductive emergencies in the male

Paraphimosis

Aetiopathogenesis

Paraphimosis is the inability to fully retract the glans penis into the prepuce. In dogs, reported causes include coitus, foreign body (including hair) entrapment, trauma, neoplasia, neuromuscular disease of the preputial muscles, inversion of the preputial skin and hair, and hypoplasia or other abnormalities of the preputial orifice. In the male cat, the disease has only been reported in association with abnormalities of the preputial orifice.

If left uncorrected, venous drainage from the glans may be affected, leading to swelling, further penile circulatory compromise, and eventually ischaemic damage. Severe swelling or ischaemic necrosis may lead to secondary urethral obstruction.

Clinical signs and diagnosis

Clinical signs include extrusion of the glans beyond the preputial orifice, usually accompanied by discomfort and excessive grooming of the penile tip (Figure 15.1). If uncontrolled, self-mutilation may result, although as ischaemic necrosis develops, the penis may become less painful and the animal may pay less attention to the area.

Therapeutic interventions

The aim of treatment is to return the penis into place within the prepuce and prevent further prolapse. Gentle cleansing, surface cooling and lubrication is frequently all that is required, although many animals will require chemical restraint and systemic analgesia to permit manipulation and reduction. The use of topical agents to reduce swelling pre- and post-reduction has been described, although this appears unnecessary in most cases. Occasionally, surgical enlargement of the preputial orifice may be necessary to allow reduction of the organ, and in extreme cases phallopexy or partial penile amputation may be required. A temporary purse-string suture in the preputial orifice following reduction may be placed, and consideration should be given to the use of systemic anti-inflammatories. Identification and correction of the underlying aetiology is mandatory.



15.1 Paraphimosis in an English Bulldog. (Courtesy of RA Goggs)

Priapism

Aetiopathogenesis

Priapism is the presence of persistent penile erection in the absence of sexual stimulation. It can be caused in two ways: high-flow priapism, where arterial inflow to the penis exceeds the compensatory venous drainage mechanisms; and low-flow priapism, where venous outflow is reduced, leading to an accumulation of stagnant blood within the penis. Low-flow priapism, secondary to ischaemic, neurogenic or occlusive (both intra- and extravascular) disorders, is far more common in companion animals. Some physiological differences exist, with blood accumulating in

the corpus cavernosum in cats and the corpus spongiosum in dogs, although these differences are of little clinical relevance. Causes include trauma, neurological disorders, drug administration (amphetamines, psychotropic drugs), neoplasia, lower urinary tract diseases and thromboembolic disorders.

Clinical signs and diagnosis

Clinical inspection is often sufficient to make the diagnosis, although a consistent history of trauma or evidence of neurological disease may exist (Figure 15.2). Low-flow priapism appears initially to be painful, although pain may diminish as ischaemic damage progresses. If no obvious cause is apparent, full physical examination is indicated to rule out the possibility of systemic disease resulting in secondary thromboembolic complications.



15.2 Priapism in a Weimaraner. (Courtesy of RA Goggs)

Therapeutic interventions

The degree of intervention required often depends upon the longevity of the priapic state. Initially, surface cooling together with compression massage may be sufficient, although aspiration of corporal blood will often be required: via a lateral approach, blood should be aspirated until 'fresh blood' is obtained (Figure 15.3). Local administration of vasoactive agents (such as phenylephrine) to cause vasoconstriction has been described, although the risk of penile hypoperfusion and consequent ischaemic necrosis should be considered. If the priapic state persists for more than 36 hours, surgical intervention is indicated, and may range from multiple Tru-cut needle 'coring' of the affected corpus (equivalent to the Winter's shunt technique in human medicine), to creation of a corporo-venous shunt (analogous to the Grayhack or Barry techniques) or penile amputation.



15.3 Aspiration of blood to treat priapism. (Courtesy of S Cortellini)

Testicular torsion

Aetiopathogenesis

The aetiology of this condition is incompletely understood at present, although it is believed to occur secondary to rupture of the scrotal ligament. Effectively, axial rotation of the testis on the spermatic cord results in venous occlusion of the pampiniform plexus, resulting in testicular swelling and ultimately ischaemic necrosis. Whilst the condition does occur in anatomically normal scrotal testes, it is encountered more frequently in association with neoplastic, abdominally retained testes. The condition has not been reported to date in the cat.

Clinical signs and diagnosis

Testicular torsion results in unilateral pain, scrotal swelling and enlargement of the affected testis and spermatic cord. Ultrasonographic examination may provide confirmation, but is rarely required. Diagnosis of intra-abdominal testicular torsion may be more challenging. These patients often present as an 'acute abdomen case', with lethargy, abdominal discomfort, vomiting and signs of systemic inflammation being the most commonly noted clinical signs. In these cases, following analgesia, resuscitation and stabilization of their cardiovascular abnormalities, abdominal imaging (including radiography and ultrasonography) is indicated. Exploratory coeliotomy may be required, and should permit a definitive diagnosis.

Therapeutic interventions

Following due consideration of systemic analgesia (see Chapter 21) and correction of any cardiovascular abnormalities (see Chapters 3 and 4), prompt surgical removal of the affected testis is indicated. Given the lack of knowledge regarding the aetiology of this condition, removal of the unaffected testis should be considered and discussed with the animal's owner prior to surgery.

Prostatitis

Aetiopathogenesis

Benign prostatic hyperplasia (BPH) is considered to be ubiquitous in middle-aged to older intact male dogs; while it is frequently subclinical, it appears to predispose animals to prostatitis, prostatic cysts or prostatic abscessation. Prostatitis and BPH are uncommon in neutered male dogs; however, this population appears to be at greater risk of prostatic neoplasia. Prostatic disease is rare in cats as this species does not seem to develop BPH. Affected animals should be thoroughly investigated as the presence of consistent clinical signs is likely to be associated with more significant disease.

The prostate gland achieves full development and growth by around 2 years of age in the dog. In the intact male, however, continuous intra-prostatic conversion of testosterone to dihydrotestosterone promotes the

ongoing hypertrophy and glandular hyperplasia of the prostate gland (BPH). Cystic hyperplasia, retention of prostatic fluids and altered vasculature predispose the gland to bacterial infection (usually ascending, although occasionally secondary to lower urinary tract infection or haematogenous spread). Once established, such bacterial infections can progress to abscess formation. Most infectious agents identified are of gastrointestinal origin (*Escherichia coli*, *Klebsiella* spp., *Enterobacter* spp.), although *Staphylococcus* spp., *Streptococcus* spp., *Mycoplasma canis* and fungal organisms have also been isolated.

Clinical signs and diagnosis

Animals affected by acute prostatitis are often systemically ill, with general signs consistent with sepsis, together with more specific signs related to the prostate; urinary/faecal tenesmus are often present, together with caudal abdominal/lumbosacral discomfort and occasionally hindlimb lameness. While rectal palpation may not always reveal an abnormal prostate, examination of the prostate is invariably painful. With an acute bacterial prostatitis, other clinical signs consistent with a lower urinary tract infection may also be present. Routine blood-work should be consistent with systemic inflammatory response syndrome/sepsis, but on occasion a degenerative neutropenia (rather than the neutrophilia seen with an inflammatory leucogram) may be present.

Following identification of consistent clinical signs, diagnostic imaging is indicated. Survey radiography is useful to highlight the size, shape and position of the prostate gland; however, in the emergency setting, ultrasonography is a more useful technique: findings may include prostatomegaly, asymmetry, irregular borders and the presence of hypoechoic, fluid-filled cavities (Figure 15.4). As acute bacterial prostatitis and prostatic abscessation can progress to septic peritonitis, the region surrounding the prostate gland should also be carefully examined for the presence of free fluid. Diagnostic samples for cytology and culture can be obtained by fine needle aspiration, although there is a risk of bacterial seeding along the needle tract; prostatic wash and brush sampling are preferable. Pre-pubic cystocentesis may also be performed, but this should not be relied upon as a sole means of diagnosis as urinary and prostatic bacterial isolates are frequently different.



15.4 Ultrasound image demonstrating multiple, irregular fluid-filled structures (abscesses) within the prostate gland.

Therapeutic interventions

Affected animals are often severely systemically ill; therapy to resuscitate and support the major body systems is therefore a priority. After obtaining diagnostic samples, targeted antimicrobial therapy should be started. The blood–prostate barrier is likely to be compromised in the inflamed state; however, agents with good penetration of the prostate gland, such as fluoroquinolones, potentiated sulphonamides and chloramphenicol, are still indicated. Obligate anaerobic infection of the prostate is uncommon, but broad-spectrum cover (e.g. the combination of metronidazole/clindamycin with a fluoroquinolone) should be maintained until culture and susceptibility results are obtained. Appropriate antimicrobial therapy should be continued for 4–6 weeks in order to minimize the likelihood of chronic bacterial prostatitis developing.

Neutering of animals affected by acute prostatitis is indicated; however, surgical castration should be avoided until the infection appears under control and the patient is systemically well. Until that point, 'chemical castration' with osaterone acetate or finasteride is indicated.

Urethral prolapse

Aetiopathogenesis

Urethral mucosal prolapse through the external urethral orifice is an uncommon finding in male dogs, most frequently identified in English Bulldogs. It has not been reported in the cat. It appears to occur most often following persistent urethral irritation, subsequent to urolithiasis, dysuria or sexual stimulation.

Clinical signs and diagnosis

Identification of everted urethral mucosa at the penile tip is pathognomonic; the tissue is usually erythematous, congested and may show signs of dessication and trauma (Figure 15.5).

Therapeutic interventions

Traditionally, resection and anastomosis of the affected portion of the urethral mucosa has been advocated. However, a recently described technique for urethropexy appears to be straightforward, reasonably effective and associated with few complications (Kirsch *et al*., 2002).



15.5 Urethral prolapse.
(Courtesy of M Tivers)

Reproductive emergencies in the non-pregnant female

Cystic endometrial hyperplasia/pyometra

Aetiopathogenesis

Cystic endometrial hyperplasia is a frequently observed state where the uterus contains numerous fluid-filled cysts and luminal glandular fluid. In pyometra, this condition appears to be exacerbated by proliferation of gastrointestinal flora within the uterus, which probably gain access during oestrus. In cats, the differing ovarian physiology (most queens are induced ovulators) leads to slightly different patterns and incidence of disease compared with dogs. The use of exogenous progestogens (for oestrus control) and oestrogens (for population control) should also be considered as a significant risk factor in the development of the condition.

Pyometra is a common disease of dioestrus, with the progesterone produced by corpora lutea during this phase permitting the development of bacterial infection. Consequently, most females begin to show clinical signs between 5 and 80 days after the end of oestrus, with the majority occurring within 5–6 weeks. Research has indicated that progesterone levels are similar in normal bitches and those with pyometra, so it seems likely that other factors play a role in disease development. The main actions of progesterone are to encourage endometrial growth, increase uterine glandular secretions, reduce myometrial contractility and decrease cervical patency, whilst oestrogens enhance the effects of progesterone. Progestogens also appear to permit enhanced bacterial adherence and reduce intrauterine neutrophil chemotaxis and phagocytosis.

Clinical signs and diagnosis

Clinical signs in pyometra, with the exception of a purulent vulval discharge, are generally attributable to the systemic effects of bacterial toxins, as well as the complex proinflammatory state this produces (see Chapter 3). Animals are invariably lethargic, with inappetence, vomiting and polyuria/polydipsia frequently noted. The reduced appetite and vomiting are usually a consequence of circulating proinflammatory mediators, although hepatic and renal dysfunction can be a factor in severely affected individuals. The polyuria/polydipsia is most commonly due to reduced antidiuretic hormone (ADH) activity in the distal convoluted tubules/collecting ducts in the kidney, although glomerulosclerosis, tubular atrophy and interstitial nephrosis have been reported (Maddens *et al*., 2011) and may play a role in the kidney dysfunction. In addition, many bitches (>20%) are found to have concurrent urinary tract infections. The vulval discharge can be extremely variable in nature and volume, and in cases of 'closed cervix pyometra' may be absent altogether: such cases frequently progress to uterine rupture and septic peritonitis and are often fatal if not diagnosed early.

The history and clinical signs are often highly suggestive, and pyrexia and an inflammatory leucogram are usually, but not universally, present. Circulating prostaglandin F metabolites can be assayed, with levels >3000 pmol/l being highly specific for pyometra. Diagnostic imaging, however, is probably the most useful technique to confirm a diagnosis: abdominal radiography and ultrasound examination usually demonstrate the presence of a fluid-filled uterus, easily differentiated from other viscera (Figure 15.6).



15.6 Ultrasound image demonstrating 'classical' appearance of fluid-filled uterine horns in pyometra.

Therapeutic interventions

Ovariohysterectomy is the treatment of choice for pyometra in bitches and queens. Some success with medical treatment is reported, although recurrence rates can be high. Many animals with pyometra will present with marked systemic signs of inflammation due to sepsis. The key to management, surgical or medical, is recognition of the condition and timely and appropriate correction of the circulatory and organ dysfunction present. Treatment of hypoperfusion, initially utilizing isotonic crystalloids, should be performed, although attention should also be paid to correction of hypoglycaemia or any electrolyte disturbances (see Chapters 4 and 5).

Broad-spectrum intravenous antimicrobial therapy should be started as soon as possible; this should be continued for 5–30 days depending on whether surgical or medical treatment is elected. Samples should be obtained for culture and antibiotic susceptibility, and antimicrobial therapy adjusted accordingly. Studies appear to indicate that *Escherichia coli* is the most common infectious agent (60–70%), although other Gram-negative organisms, as well as Gram-positive bacteria such as *Streptococcus* and *Staphylococcus* spp., are also reported. In naturally occurring pyometra antimicrobial resistance appears uncommon, indicating that antibiotics such as co-amoxiclav, second-generation cephalosporins and trimethoprim-potentiated sulphonamides are likely to be effective; agent selection, however, should be guided by local patterns of resistance and patient factors.

Medical management is frequently reserved for animals of high breeding value, although can be considered for any animals in good systemic health. Progesterone receptor antagonists such as aglepristone are often effective in stimulating cervical dilation and consequent conversion to an 'open pyometra'. The average time to achieve cervical opening is around 24 hours, so this drug has the potential to be of benefit to all animals requiring medical stabilization, even if surgical treatment is planned. As pyometra is effectively a disease of the luteal phase, the use of a prostaglandin F2 α analogue, with or without a dopamine agonist such as cabergoline, should result in luteolysis and resolution of the disease (see Figure 15.7 for a suggested protocol). Broad-spectrum antimicrobial treatment should be maintained for 30 days. The use of prophylactic antibiotics during subsequent oestrous periods has been recommended.

Drugs (as single agent)	Dose	Dosing regime
Aglepristone	10 mg/kg s.c.	Days 1, 2 and 8
Cabergoline	5 μg/kg orally	Once daily for 1 week
Dinoprost	250 μg/kg s.c.	Days 1, 2, 3, 4 and 5
Drug combinations		
Aglepristone with cloprostenol	10 mg/kg s.c. 1 μg/kg s.c.	Days 1, 2 and 8 Days 3, 5, 7, 9, 11, 13 and 15
Cabergoline with cloprostenol	5 μg/kg orally 5 mg/kg s.c.	Once daily for 1 week Days 1, 4, 7 and 10
For all patients (recommended)		
Broad-spectrum antimicrobial therapy	As per licensing information	For 30 days

15.7 Suggested treatment protocol for medical management of pyometra in bitches.

Following medical management, recurrence of pyometra is common (15–20% in queens, 20–75% in bitches), although success in subsequent pregnancies is also reported to be high, with 40–90% of bitches producing normal litters.

As indicated above, surgical management is the treatment of choice for most animals following adequate systemic stabilization. Aglepristone will usually induce cervical opening within 48 hours of administration, potentially resulting in a reduction in endotoxaemic load and physiological compromise during anaesthesia; however, potential benefits should be weighed against the risk of delaying surgery. Samples of uterine content and urine (via cystocentesis) should be obtained for bacterial culture. At coeliotomy, rupture of the uterus and gross contamination of the peritoneal space may be apparent, indicating the need for appropriate postoperative management of septic peritonitis (see Chapter 12); however, some bacterial contamination of the peritoneal space is likely in all cases. Therefore, following ovariohysterectomy, copious lavage of the abdomen with warm normal saline is recommended. Postoperatively, antimicrobial therapy should be maintained for 10 days, with other treatment and nursing care dependent upon the condition of the animal. In general, if appropriate preoperative therapy is provided, together with sound surgical technique and postoperative care, a good prognosis should be expected.

Vaginal hyperplasia

Aetiopathogenesis

Vaginal hyperplasia (frequently mistaken for prolapse) is the development of hyperplasia and oedema in the normal mucosal tissue in the caudal vagina secondary to circulating oestrogens. It is therefore almost always present only during oestrus and will resolve as oestrogen concentrations decrease. If the mass becomes excessively large, the external urethral orifice may become obstructed, resulting in dysuria. The tissue protruding through the vulval lips can be of concern to the bitch and excessive licking may lead to severe self-trauma. The condition has, to date, not been reported in the queen.

Clinical signs and diagnosis

The clinical appearance of a smooth, pink mass protruding from the vulva of a bitch in oestrus is pathognomonic (Figure 15.8). A full history and clinical examination should still be performed, however, in order to determine whether the exposed mucosa is necrotic and to detect any evidence of urethral obstruction.



15.8 Vaginal hyperplasia in a Staffordshire Bull Terrier. (Courtesy of M Tivers)

Therapeutic interventions

Frequently, gentle cleansing and lubrication is sufficient; an Elizabethan collar should be used to prevent self-trauma. Whilst the condition will resolve naturally given time, the administration of progestagens to accelerate the termination of oestrus is often advisable. Ovariohysterectomy during the subsequent anoestrus period will prevent recurrence. In extreme cases, or those with excessive necrosis of the protuberant mucosa, surgical resection is sometimes necessary. Access to the caudal vagina/vestibule is enhanced by performing an episiotomy, allowing resection of the hyperplastic tissue. Such surgery is usually accompanied by considerable blood loss and pre-placement of a urinary catheter is strongly recommended to act as a landmark and to assist in prevention of iatrogenic urethral damage.

Reproductive emergencies in the pregnant female

Hypocalcaemia

See Reproductive emergencies of the postparturient female below for information.

Hypoglycaemia

Aetiopathogenesis

Rarely, bitches may present with hypoglycaemia prior to parturition. The underlying pathogenesis has yet to be determined, but is unusual in that the high levels of progesterone present during pregnancy should produce peripheral insulin antagonism, resulting in hyperglycaemia. The condition has not been reported in the queen.

Clinical signs and diagnosis

Signs of muscle weakness progressing to seizure and coma are usually present: such cases are often mistaken for hypocalcaemic animals, although hyperthermia and

tetany are rarely noted. Blood glucose should be measured as part of the initial emergency database in any collapsed animal. Failure to respond to appropriate treatment for presumed hypocalcaemia should prompt a re-evaluation of the case and determination of the blood glucose level.

Therapeutic interventions

Administration of intravenous glucose to effect will usually result in rapid resolution of signs; a dose of around 0.5 g/kg (1 ml/kg 50% dextrose solution) diluted in 0.9% saline solution to give a final concentration <10% dextrose will usually be effective. Ongoing intravenous supplementation is occasionally required, although frequent feeding with an energy-dense diet is usually sufficient to prevent recurrence until parturition.

Hyperglycaemia

Aetiopathogenesis

High levels of circulating progesterone are present during pregnancy. Progesterone has an antagonistic effect on insulin and also stimulates the release of growth hormone. The direct effect of the progesterone is to reduce peripheral insulin binding and therefore glucose uptake into cells, whereas the increased level of growth hormone causes down-regulation of insulin receptors and inhibition of glucose transport. Development of novel diabetes mellitus may therefore occur in the pregnant bitch (the condition appears rare in the queen), and in addition pregnancy may induce instability in glycaemic control in previously diagnosed diabetic cases.

Clinical signs and diagnosis

Clinical signs and diagnosis of hyperglycaemia are discussed in detail in Chapter 16.

Therapeutic interventions

Treatment of hyperglycaemia (and other allied conditions) associated with diabetes mellitus is discussed in Chapter 16. In pursuing treatment of such cases, due consideration should be given to the health of the fetuses and the effect of any systemic treatment given.

Dystocia

Timing of normal parturition

When presented with a case of potential dystocia in dogs or cats, certain species variations in physiology are worth remembering. Queens are seasonally polyoestrous, with (induced) ovulation taking place 24–48 hours after mating. Gestation length is consistently 63–65 days, so the timing of parturition following any planned pregnancy in the cat can be reasonably accurately predicted. Prolongation of gestation beyond these times in the queen invariably reflects unnoticed dystocia or uterine inertia.

In contrast, length of gestation in the bitch can be extremely variable, with pregnancies of 58–72 days following mating considered normal. This difference is due to variation in canine oestrous behaviour, timing of ovulation within oestrous, prolonged pre-implantation 'life span' of oocytes, and variability in the viability of sperm within the female reproductive tract. If mating was planned, canine gestational length can be fairly accurately predicted to be 64–66 days from the surge in luteinizing hormone during ovulation.

As mating in dogs and cats is frequently unplanned and not witnessed, such measures can unfortunately be difficult to use in practice. In both bitches and queens, however, luteolysis results in a reduction in plasma progesterone levels around 24–36 hours prior to parturition. In the normally pregnant queen or bitch, therefore, progesterone levels are high, whereas a low level indicates that parturition is impending, or should already have taken place. Absence of signs of parturition in such circumstances should prompt full evaluation of the dam, as well as ultrasound examination to assess fetal health. Primary uterine inertia may be present, in which case urgent veterinary intervention may be required. In addition, rectal temperature in the bitch reduces by at least 1°C 12–24 hours prior to birth. If prolonged gestation or uterine inertia is a concern, attentive owners can be advised to check their bitches' rectal temperature twice daily in the last 2–3 weeks of pregnancy.

The first stage of labour is often subtle, consisting of intermittent mild uterine contractions, together with cervical dilatation and behavioural changes. Stage 1 generally persists for 6–12 hours in the bitch, although can be less predictable in the queen.

During the second stage of labour, myometrial activity intensifies (both in strength and frequency), and is accompanied by voluntary abdominal contractions; fetal entry into the birth canal frequently results in rupture of the allantochorionic membranes, resulting in a clear vaginal discharge. Stage 2 labour usually lasts for 3–12 hours in dogs and cats, although it can be prolonged for over 24 hours without apparent fetal harm. During Stage 2, consecutive fetuses are usually delivered within 2 hours of each other, but viable neonates can be obtained after longer intervals.

Classically, Stage 3 of labour consists of the expulsion of fetal membranes; in bitches and queens this is often interspersed with the delivery of viable fetuses, but is usually considered complete once uterine involution has commenced.

Aetiopathogenesis of dystocia

Dystocia is generally classified as functional (non-obstructive) or obstructive. Functional dystocia is usually termed uterine inertia and is categorized as primary, probably the most common cause of dystocia in dogs and cats, or secondary. Causes of uterine inertia are many and varied: the common reasons are highlighted in Figure 15.9. Although other aetiologies are possible, secondary uterine inertia most frequently occurs following obstructive dystocia. Obstructive dystocia is divided into maternal and fetal causes, although often a combination of factors is present. Common reasons for obstructive dystocia are indicated in Figure 15.9, with more in-depth information in the References and further reading section at the end of this chapter.

Clinical signs and diagnosis

Signs of primary uterine inertia can be difficult to identify: if the second stage of labour does not commence, the first easily observable signs may be an increased volume of green-coloured vulval discharge as placental separation takes place. If untreated, the dam may become systemically ill as the undelivered fetuses begin to decompose. If the expected due date is known, or if an observant owner notices failure to progress beyond the first stage of labour, the condition may be detected more easily.

Causes of primary uterine inertia
• Electrolyte abnormalities (hypocalcaemia, hypomagnesaemia) • Stress • Age • Obesity • Uterine overdistension due to large litter size • Inadequate fetal cortisol due to small litter size • Myometrial abnormalities • Oxytocin deficiency • Systemic illness
Causes of secondary uterine inertia
• Obstructive dystocia • Pain • Fatigue • Diaphragmatic rupture • Uterine rupture • Abdominal wall rupture • Tracheal rupture
Causes of maternal obstructive dystocia
• Ectopic pregnancy • Uterine adhesions • Uterine herniation • Reduced cervical dilatation • Reduced pelvic diameter • Obesity • Uterine torsion • Vaginal/vulval abnormalities
Causes of fetal obstructive dystocia
• Abnormal fetal posture • Abnormal fetal position • Abnormal fetal presentation • Absolute fetal oversize • Fetal developmental abnormalities • Fetal death

15.9 Causes of functional and obstructive dystocia in dogs and cats.

Other signs of dystocia generally include failure to deliver a fetus following prolonged (>20 minutes) active straining, the presence of an undelivered neonate at the vulva or *per vaginam* and evidence of maternal distress or fatigue before the predicted end of parturition. Clinical indications for veterinary examination and intervention are detailed in Figure 15.10.

Abdominal imaging can be of great value in evaluating potentially dystocic dams: fetal numbers can be identified radiographically as both canine and feline neonates begin skeletal calcification at around 45 days of gestation.

Indications for veterinary intervention
• Abnormal vaginal/vulval discharge • No onset of Stage 2 labour (primary uterine inertia) • Stage 2 labour >4 hours without fetal delivery • >2 hours between fetal deliveries • >30 minutes active straining without fetal delivery • >1 hour weak intermittent straining without fetal delivery • Evidence of maternal distress • Evidence of fetal distress (heart rate <180 bpm or <2 x maternal heart rate)
Indications for surgical intervention
• No onset of Stage 2 labour (primary uterine inertia) • Non-obstructive uterine inertia refractory to medical treatment • Feto-maternal disproportion • Systemic maternal illness • Evidence of maternal distress refractory to medical treatment • Evidence of marked fetal distress (heart rate <150 bpm) • Prolonged Stage 2 labour with multiple fetuses in absence of obstruction

15.10 Key indications for veterinary intervention in dystocia.

Abdominal ultrasound examination can similarly be useful in estimating litter size, but more importantly can be employed to determine fetal heart rate during parturition: fetal heart rates should generally be at least twice that of the dam, with rates less than 150 bpm indicating likely fetal distress and a need for rapid intervention.

Therapeutic interventions

Treatment of dystocia is divided into medical and surgical. Broad indications for Caesarean section can be difficult to apply in individual animals; however, some guidelines are presented in Figure 15.10. It is often suggested that if a Caesarean section is being considered, it probably should be performed. Whilst much emphasis is placed on direct therapy of the dystocia, it should also be remembered that many periparturient dams will be weak, fatigued, dehydrated and potentially hypocalcaemic and hypoglycaemic. While delivery of any remaining fetuses should not be delayed unduly, treatment should also be directed at stabilizing the systemic condition of the dam.

Medical treatment should only be pursued if vaginal examination (and abdominal imaging, if required) fails to indicate an obstructive component to the dystocia. The mainstays of medical management are administration of exogenous oxytocin analogues (to increase frequency of myometrial contraction) and intravenous calcium (to increase the strength of myometrial contractions); the latter may well be indicated even in the absence of documented hypocalcaemia. High doses of oxytocin lead to uncoordinated tetanic uterine contractions that may result in further fetal distress: the recommended dose is therefore 0.1 IU/kg up to a maximum of 5 IU, injected intramuscularly. The half-life of oxytocin is around 5 minutes so repeated doses every 30–40 minutes may be required if multiple undelivered fetuses are present. If the dam is normocalcaemic, slow intravenous supplementation of calcium (0.25 ml/kg of 10% calcium gluconate solution, diluted with 0.9% saline solution) can be considered. High levels of calcium supplementation can lead to excessive myometrial contractions in parturient queens and so should be used with caution. If assisted vaginal extraction of neonates is required, gentle traction (digital initially, then with obstetric instruments) together with copious amounts of water-soluble lubricants are essential: the use of feline urinary catheters to instil lubricant into the birth canal can be useful to assist the expulsion of vaginally obstructive fetuses.

If surgical intervention is indicated, it should be remembered that pregnancy, as well as dystocia, has significant effects upon the dam's physiology: blood volume and cardiac output are increased; minute ventilation and oxygen consumption are increased; functional lung capacity is reduced and gastric emptying is delayed. These factors, together with the urgency of the situation, conspire to create a significant anaesthetic risk for these patients; in addition, any drugs administered need to be considered in light of their effects upon not only the dam, but on the neonates as well.

Prior preparation of the dam to minimize anaesthetic time is vital; intravenous access should be obtained and fluid therapy initiated, and the patient surgically clipped as far as possible before induction. Drug choice is subjective and the reader is directed to the *BSAVA Manual of Canine and Feline Anaesthesia and Analgesia* for a more in-depth discussion of the subject. However, current recommendations are that potent sedative agents such as phenothiazines and alpha-2 agonist drugs be avoided,

pre-medication with anticholinergics such as atropine is not indicated, and administration of potent or long-lasting opioids should be delayed until after delivery of the neonates has been completed. Induction with ultra-short acting-barbiturates, propofol, alfaxalone or volatile agents appears acceptable in most circumstances, although it should be remembered that most of these agents will cross the placenta and dosages required for pregnant animals can be unpredictable.

Other induction protocols such as benzodiazepine/ketamine combinations have been described and, while certain anaesthetic protocols may have theoretical comparative advantages in a compromised patient such as a periparturient female, familiarity with the anaesthetic technique utilized is probably of greater importance. Pre-oxygenation for 5–10 minutes prior to induction is advisable, and following loss of the gag reflex the dam should be maintained in sternal recumbency until an endotracheal tube is placed and secured, owing to the likelihood of gastric reflux. The use of local anaesthetic blockade or epidural/extradural opioid administration can be beneficial, although care should be taken to ensure duration of anaesthesia is not unduly extended.

Caesarean section

A full discussion of the surgical techniques involved in performance of successful Caesarean sections is beyond the scope of this publication, and interested readers are directed towards the *BSAVA Manual of Canine and Feline Reproduction and Neonatology*. However, some useful guidelines can be given here.

In most circumstances, a ventral midline approach is recommended for surgeon familiarity; however, tilting of the dam out of true dorsal recumbency may relieve pressure on the major abdominal vessels from the gravid uterus and therefore be beneficial for cardiovascular stability. Typically, a single incision is made in the body of the uterus and the fetuses are 'milked out' sequentially; however, in some patients an incision in each uterine horn may be required. Following removal of the fetuses, firmly attached placentae should be left *in situ*; great care should be taken to explore the entire length of the uterine horns to ensure no fetuses remain, and the pelvic canal should similarly be carefully examined, both from the peritoneal cavity and *per vaginam*. Whilst experimentally the canine uterus appears able to heal without suturing, closure with 1–2 layers in an inverting pattern is recommended. Uterine knots should be buried if possible, to reduce future adhesions. Lavage and suction of the peritoneal cavity with warm sterile saline solution is advised following uterine closure. If uterine involution does not occur following closure of the uterine incision, low-dose oxytocin should be administered. Routine abdominal closure is followed, although the use of cuticular ('intradermal') sutures may result in a lower risk of wound breakdown as a result of interference from nursing neonates.

In certain circumstances, ovariohysterectomy may be performed at the same time as Caesarean section: owners should be advised that it is possible that this procedure may carry greater morbidity than separation of the two procedures, although it will not affect lactation. Similarly, *en bloc* resection of the uterus prior to delivery of individual fetuses is described (MacPhail, 2013): it should be remembered that if carried out, the time from application of the first uterine vascular clamp to removal of the final fetus from the uterus should not exceed 60 seconds, otherwise fetal viability is likely to be adversely affected. If fetal compromise is present prior to anaesthesia, this technique is contraindicated.

Following Caesarean section or successful medical management of dystocia, consideration should be given to postparturient care. For the dam, broad-spectrum antimicrobial coverage is advisable for 7–10 days and analgesia should be provided. Both opioids and non-steroidal anti-inflammatory drugs (NSAIDs) cross the blood–milk barrier, but at low levels, and are unlikely to carry much risk of adverse effects in the nursing neonates. Selective COX-2 inhibitor drugs are relatively contraindicated in human paediatric medicine, however, and therefore may best be avoided. It should be remembered that few therapeutic agents are licensed for use in lactating females or neonates, and informed consent should always be obtained from a client before any such 'off-label' drug use is considered.

Reproductive emergencies in the postparturient female

Hypocalcaemia

Aetiopathogenesis

Puerperal tetany or eclampsia is most commonly identified in late pregnancy or early lactation in small to medium size bitches, and occasionally in early lactation in multiparous queens. The likely pathogenesis is the combination of reduced dietary consumption/availability and increased calcium loss in the milk. The concurrent presence of hypoglycaemia is associated with increased calcium binding to protein, reducing the level of ionized calcium and potentially exacerbating the condition.

Clinical signs and diagnosis

Calcium has significant biochemical roles in all cells, but particularly those whose function depends upon membrane excitability. Clinical signs initially involve restlessness, tachypnoea and ptyalism, but will rapidly progress to generalized muscle weakness, muscle fasciculations, hyperthermia and dysrhythmias. Seizures, tetany, hypotension and death are the eventual sequelae if the condition remains untreated (see Chapter 5).

Suspicion should be raised by the history and clinical signs, although the demonstration of hypocalcaemia (total calcium <2.0 mmol/l in dogs, <1.75 mmol/l in cats; ionized calcium <1.25 mmol/l in dogs, <1.1 mmol/l in cats) is required for confirmation. At the time of presentation, most eclampsic animals are severely hypocalcaemic (total calcium <1.6 mmol/l, ionized calcium <0.8 mmol/l). As the two conditions are frequently encountered together, blood glucose levels should also be checked to allow detection and treatment of hypoglycaemia if present.

Therapeutic interventions

Emergency therapy involves the slow intravenous administration of calcium gluconate to effect. A dose of around 10 mg/kg calcium is usually effective: this equates to 1 ml/kg of 10% calcium gluconate solution, diluted with 0.9% saline and given over 15–20 minutes. Ideally, an electrocardiogram should be monitored during administration, but if unavailable, palpation of peripheral pulse rate, rhythm and quality may be sufficient.

The beneficial effect of this treatment will persist for 2–12 hours, therefore ongoing support will be required. A short period of intravenous supplementation should help restore some of the depleted calcium stores in the body, but oral supplementation may be required as well. Preventative administration of calcium supplements in very late pregnancy and early lactation may be beneficial, as excessive oral calcium ingestion does not appear to reduce parathyroid hormone levels in the periparturient bitch or queen. If appropriate, consideration should be given to early weaning of the neonates or provision of artificial milk substitutes.

Retained fetuses/fetal membranes

Aetiopathogenesis

True retention of placentae is uncommon in dogs and cats experiencing normal parturition, despite being of frequent concern to owners. Retention of fetuses or fetal membranes is almost invariably the sequela of uterine inertia, and should be considered a potential consequence of any episode of dystocia.

Clinical signs and diagnosis

Clinical signs of retained fetuses/fetal membranes include persistence of copious (usually green-tinged) vaginal discharge beyond 12–24 hours postpartum (a low-volume green vaginal discharge can be normal for up to 3–6 weeks). Systemic illness usually develops rapidly in bitches, although this may take several weeks in the queen. Definitive diagnosis can be difficult: ultrasonographic detection of retained fetal membranes can be challenging in the immediately postparturient uterus and abdominal palpation misleading. Abdominal radiography can be useful in detection of fetal skeletons, but may not assist in identifying retention of placentae.

Therapeutic interventions

Stabilization of the affected dam with intravenous fluids and systemic antimicrobial agents is indicated. If retained fetal membranes are suspected, then administration of exogenous oxytocin may be required to induce expulsion. If medical management is successful, these patients should be considered at high risk for development of metritis and administered broad-spectrum antimicrobial agents for 30 days. Persistence of the vaginal discharge despite medical treatment, and the radiographic/ultrasonographic detection of retained fetuses, necessitates surgical intervention: hysterotomy to remove non-expelled uterine contents may be sufficient; however, if future breeding potential of the dam is of little concern then ovariohysterectomy is the treatment of choice.

Metritis

Aetiopathogenesis

Acute metritis is a postparturient bacterial infection of the uterus, usually due to contamination with endogenous gastrointestinal microflora. Various problems predispose to the condition, including dystocia, obstetric intervention, retained fetuses or placentae and poor uterine involution postpartum.

Clinical signs and diagnosis

As the infection usually begins soon after parturition, many females with acute metritis progress to systemic illness quite rapidly. Most are lethargic and anorexic initially but will become weak, hypoperfused and collapsed if the condition is not recognized and treated early. A serosanguineous or purulent vaginal discharge is frequently present. Haematological testing will usually reveal an inflammatory leucogram. Diagnostic imaging is extremely useful, with abdominal ultrasonography often able to demonstrate an enlarged uterus with thickened walls and echogenic intraluminal content.

Therapeutic interventions

As many bitches and queens with metritis will be systemically ill, the initial therapeutic concern is to re-establish cardiovascular stability using intravenous fluid therapy as necessary. Systemic broad-spectrum antimicrobial therapy is indicated, and should be continued for around 30 days. Samples of the vaginal discharge should be submitted for bacterial culture to determine the most appropriate long-term choice of agent. Unlike pyometra, no underlying endocrine state exists in metritis, so hormonal intervention is of minimal use. However, ecbolic agents such as oxytocin and prostaglandin analogues can be used to encourage involution and drainage of the uterine contents. Lavage of the uterine lumen using warm 0.9% saline solution has been shown to be of benefit and intraluminal administration of antimicrobial agents may also be of use. If the condition fails to improve with medical management, however, ovariohysterectomy is indicated.

Uterine haemorrhage

Aetiopathogenesis

Postpartum haemorrhage is an uncommon condition of the bitch and queen and is usually a result of trauma to the uterus or birth canal, often of iatrogenic origin. Placental necrosis can result in uterine haemorrhage, but is rare. It should be remembered that a small volume of sanguineous vulval discharge is normal after parturition; this will rapidly reduce in volume, however, and will generally progress from red to green in colour over the first few days postpartum. Any sustained haemorrhagic vulval discharge, together with systemic signs of blood loss, should prompt further action, together with investigation of the coagulation status of the animal.

Clinical signs and diagnosis

Clinical signs can vary from those of the normal postparturient bitch or queen, to signs of hypoperfusion and progressive anaemia in patients with ongoing blood loss. While frequently non-diagnostic, comparison of the peripheral haematocrit with the packed cell volume (PCV) of the discharging fluid may give some evidence as to whether ongoing haemorrhage is occurring. Palpation and direct visualization of the birth canal may indicate a site of injury or evidence of uterine blood passing through the cervix. Ultrasound examination of the abdomen may also be of benefit, although can be difficult to interpret.

If a diagnosis of uterine haemorrhage can be made with confidence, it is advisable to investigate the dam for evidence of coagulation disorders, as well as performing blood typing in case of the need to administer blood products.

Therapeutic interventions

Maintenance of cardiovascular stability is vital in these cases; this not infrequently requires the administration of

intravenous fluids and occasionally the use of blood products. Acute intervention to prevent ongoing blood loss is performed by either direct pressure, placement of vaginal tampons or local application of vasoconstrictive agents in the case of vaginal injury, or by the use of oxytocin to encourage uterine involution in the case of uterine haemorrhage. Failure to control haemorrhage via medical management indicates a need for surgical intervention; an episiotomy may be necessary to facilitate access to vaginal injuries and ovariohysterectomy may be the only realistic option to control uterine haemorrhage.

Uterine prolapse

Aetiopathogenesis

Uterine prolapse is uncommon in dogs and cats and is always associated with either parturition or abortion of fetuses. The underlying aetiology is unclear, but is likely to relate to ligament laxity of the gravid uterus, together with extensive tenesmus associated with dystocia. There is the potential for rupture of the uterine vessels during prolapse, with consequent haemoperitoneum and hypovolaemia. Uterine prolapse may be unilateral or bilateral; if unilateral prolapse occurs during parturition, it should be remembered that viable fetuses may still be present in the other (non-prolapsed) horn.

Clinical signs and diagnosis

Physical examination is usually pathognomonic: the presence of one or both uterine horns protruding from the vulva is easily distinguishable from other differential diagnoses (Figure 15.11). The dam may continue to strain, particularly if undelivered fetuses are present in a non-prolapsed horn. If prolapse has resulted in rupture of uterine vessels or severe trauma to the uterine wall, then signs of hypovolaemic shock may be present.



15.11 Uterine prolapse in a cat.

Therapeutic interventions

If signs of hypoperfusion are present, stabilization of the cardiovascular system is the priority. Significant blood loss may require the timely use of blood products, or consideration of aseptic peritoneal drainage and autotransfusion. Correction of the prolapse is surgical in nature: the prolapsed horn(s) can be manually reduced and hysteropexy performed via coeliotomy; amputation of the prolapsed horn can be attempted; or ovariohysterectomy can be performed with or without prior reduction of the prolapse. If ovariohysterectomy is not performed, a prolonged course of broad-spectrum antimicrobials is recommended to reduce the likelihood of metritis.

Mastitis

Aetiopathogenesis

Acute mastitis presents occasionally in postpartum bitches, but is less frequently encountered in queens. Reports of mastitis during pseudopregnancy in the bitch have been published (Murai *et al.*, 2013). The condition develops following the introduction of bacteria (most commonly *E. coli*, staphylococci and beta-haemolytic streptococci) into the teat and appears more frequently in dams with low mammary gland carriage and those housed in suboptimal conditions. Initial infections can be minor, although if untreated may progress to sepsis with marked systemic illness. In later stages abscess formation and gland necrosis can be seen.

Clinical signs and diagnosis

The affected gland(s) are hot, swollen and painful. The degree of pain present may lead to reduced nursing of the neonates, with their failure to thrive an inevitable consequence. With severe acute mastitis, the dam may present with marked systemic signs of inflammation and hypoperfusion. Normal canine and feline milk is yellow-white in colour, slightly acidic, with a high leucocyte content: milk from dams with mastitis is abnormal in appearance, commonly with a bloody appearance. Mastitic milk is also highly cellular; however, unlike normal milk it contains large numbers of free and intracellular bacteria. Samples for bacterial culture and antimicrobial susceptibility should be obtained if possible. Systemic manifestations of acute mastitis include an inflammatory leucogram (or occasionally a de-generative left shift), together with biochemical evidence that suggests dehydration, hypovolaemia or hypoperfusion of vital organs.

Therapeutic interventions

Correction of any systemic cardiovascular compromise is the priority, with early initiation of broad-spectrum antimicrobial cover. In those dams that will permit it, continued nursing and hot compresses will encourage removal of the purulent material, but if gland necrosis or systemic illness is present, early weaning of the neonates with ongoing artificial feeding should be seriously considered. In such cases, hot compresses and gentle manual 'stripping' of the glands should be performed several times daily.

Antimicrobial choice should initially be determined by whether the neonates will continue to feed, and latterly by the bacterial culture results. If the dam is nursing, then co-amoxiclav or a second-generation cephalosporin are the drugs of choice. If the neonates are to be removed due

to glandular necrosis or the presence of severe systemic illness, other antimicrobials – those with high lipid solubility and a neutral/weakly basic nature – are preferable: in this instance a combination of a fluoroquinolone and clindamycin is the authors' preference (see Chapter 23).

In severe cases of necrosis and abscess formation, lancing and drainage of the affected gland(s) are indicated. Prolonged medical management and careful attention to wound management may result in a good cosmetic outcome; however, surgical resection of the affected gland is often the treatment of choice. Ideally, surgery should be delayed until the initial inflammatory reaction has subsided and any systemic illness has resolved, although in severely septic patients it may be necessary to consider resection of necrotic tissue in order to achieve stabilization of the patient.

Paediatric emergencies

Paediatric emergencies are common in small animal practice. The term paediatric is used to describe animals between birth and 12 weeks of age, although this period is sometimes extended to 6 months of age. This period can be further divided into neonates (birth to 2 weeks), infants (2–6 weeks) and juveniles (6–12 weeks).

Successful treatment of paediatric dogs and cats presenting with life-threatening conditions requires knowledge of common pathological conditions and diseases as well as an understanding of the unique physiological, biochemical and haematological differences between paediatric animals and their adult counterparts. Paediatric patients can decompensate quickly and obtaining an exact diagnosis for their underlying condition can often be challenging. An understanding of common emergency conditions and diseases seen at this life stage allows the veterinary surgeon (veterinarian) to quickly institute life-saving therapy and formulate a diagnostic and therapeutic plan. In an epidemiological study on the cause of death of dogs in North America (Fleming *et al*., 2011), infectious disease and trauma were the most common causes of death in juvenile animals, and congenital abnormalities were the third leading cause of death.

The normal paediatric patient

There are many physiological differences between the normal paediatric patient and its adult counterpart. In addition, there are differences in normal haematological and biochemical values, and the lack of abdominal body fat, resulting in loss of radiographic serosal detail, makes diagnostic imaging challenging. Throughout this chapter, physiological differences between the paediatric patient and the adult will be noted.

Normal physical examination findings in a healthy neonate include a strong suckle reflex, adequate rooting behaviour (the ability to move the head in search of milk) and the ability to right itself when placed on its back. A normal neonate should be constantly nursing and sleeping for the first 2–3 weeks of life. The eyes should open at around 12–14 days and a menace reflex is not present until 2–3 months. See Figure 15.12 for a summary of normal vital parameters and some of the normal haematological and biochemical parameters in paediatric animals.

Parameter	Canine	Feline
Temperature	35.2–37.2°C (95.4–98.6°F) at birth, normalizing to adult temperatures by 28 days	36.1–36.7°C (97.98°F) at birth, 37.8°C (100°F) at 1 week
Heart rate	200 bpm	>200 bpm (range 220–260 bpm)
Respiratory rate	30 breaths/minute (respiratory rate lower within 1 hour of birth)	30 breaths/minute (respiratory rate lower within 1 hour of birth)
Haematocrit	47.5% at birth 29.9% at 28 days	35% at birth 27% at 4–6 weeks
Urine specific gravity	<1.020 until 10 weeks of age	<1.020 until 10 weeks of age
Alkaline phosphatase (ALP)	3845 IU/l (normal adult range: 4–107 IU/l)	123 IU/l (normal adult range: 9–42 IU/l)
Gamma-glutamyltransferase (GGT)	1111 IU/l (normal adult range: 0–7 IU/l)	1 IU/l (normal adult range: 0–4)
Albumin	18 g/l at 24 weeks (normal adult range: 21–23 g/l)	21 g/l (normal adult range: 23–30 g/l)

15.12 Selected normal paediatric parameters.

Common emergency conditions

Hypoglycaemia

Low blood glucose can develop rapidly in paediatric patients when there is decreased oral intake of food, sepsis, or both. This can occur due to poor husbandry when there is insufficient frequency of feedings, or secondary to gastrointestinal tract disease or infection. Hypoglycaemia can result in mild to severe clinical signs such as lethargy, depression, vomiting, inability to walk or stand, seizures, coma and death. These clinical signs develop because the brain has an obligatory need for glucose as an energy source. In addition, the neonatal myocardium uses carbohydrate-glucose (rather than long-chain fatty acids in the adult) as an energy source.

The paediatric patient has a limited ability to respond to hypoglycaemia due to an underdeveloped counter-regulatory response: insufficient release of adrenaline (epinephrine), noradrenaline (norepinephrine), cortisol and growth hormone when blood sugar is low. In addition, immature hepatic gluconeogenesis, limited hepatic glycogen stores and loss of glucose in the urine contribute to the maintenance of hypoglycaemia. Renal glucose reabsorption does not occur until after 3 weeks of age in puppies.

Gastrointestinal tract disease

Vomiting and diarrhoea secondary to gastrointestinal disease is common in paediatric patients. Common causes for gastrointestinal tract disease include viral infections (parvovirus, canine distemper virus (dogs), panleucopenia (cats), coronavirus), bacterial infections, intestinal parasites, overfeeding with formula milk, abnormal flora secondary to antibiotic administration, and foreign body ingestions/obstructions. Small intestinal intussusception is also a potential complication of gastrointestinal tract disease in paediatric patients.

Dehydration and hypovolaemia

Severe dehydration, most commonly developing from gastrointestinal tract losses or decreased oral intake, can lead to decreased intravascular volume and hypovolaemia. Decreased tissue perfusion from hypovolaemia results in decreased tissue oxygen delivery and can lead to organ failure and death if left untreated. Due to immaturity of the autonomic nervous system, paediatric patients have a limited ability to increase heart rate, contractility and systemic vascular resistance in an attempt to improve stroke volume, cardiac output and blood pressure in hypovolaemic states. In a longitudinal study examining the circulatory dynamics of puppies, heart rate rather than total peripheral resistance was responsible for generating arterial blood pressure. As puppies mature, heart rate decreases while total peripheral resistance increases, reaching adult levels at around 7 months. The development of concurrent hypothermia (see below) may depress the heart rate, which further contributes to poor tissue perfusion. Finally, the kidneys have limited ability to concentrate the urine (maximal urine-concentrating ability is not seen until approximately 10 weeks of age), which perpetuates the hypovolaemic state.

Assessing a paediatric patient for dehydration and hypovolaemia can be challenging. Skin turgor cannot be used to assess for dehydration because there is increased skin elasticity compared with adults. Therefore, mucous membranes (moist *versus* dry in dehydration) and serial measurement of bodyweight are more accurate means of assessing hydration status. However, it must be noted that mucous membranes may still be moist in patients that are significantly dehydrated. Therefore, veterinary surgeons should err on the side of assuming that a paediatric animal is dehydrated and potentially hypovolaemic when there is a history of decreased intake of food and water and/or when gastrointestinal signs are present.

Hypothermia

Sick paediatric patients are prone to development of hypothermia. Hypothermia is defined as a rectal temperature that is <35°C at birth, <35.6°C at 1–3 days or <37°C at 1 week. The lower body temperature seen in neonates is because of an overall lower amount of white fat; paediatric patients have mostly brown fat rather than insulating white fat and a large surface area to size ratio. Body heat in the neonate is generated primarily through normal daily metabolism and at least initially the neonate cannot shiver to generate additional heat. However, once the neonate reaches 6–8 days, shivering can help with endogenous heat production in conditions of hypothermia. Full adult temperature and autoregulation occurs by 28 days in dogs.

Malnutrition

Normal weight gain in puppies is 2.2 g/kg of expected adult weight/day whereas normal weight gain in kittens is 7–10 g/day. Malnutrition should be suspected in a paediatric patient with failure to gain weight, signs of constant crying, and reluctance to nurse. Malnutrition may occur secondary to insufficient milk production by the dam, poor husbandry, concurrent disease resulting in limited food intake, or malabsorption.

Respiratory distress

Aspiration pneumonia is the most common cause of respiratory distress in the neonatal patient. This could occur secondary to tube feeding or from a congenital abnormality such as a cleft palate. In the older paediatric patient (infant or juvenile), infectious causes of pneumonia and traumatic injuries (electrocution or pulmonary contusions) should also be considered as differential diagnoses in animals presenting with clinical signs of respiratory distress. Infectious causes of pneumonia include *Bordetella bronchiseptica*, canine distemper virus, parainfluenza, and canine influenza virus. Clinical signs of respiratory distress include increased respiratory rate and effort, coughing, nasal discharge, extended head and neck, cyanosis, and distended abdomen resulting from aerophagia.

Emergency approach to the paediatric patient

Initial patient assessment should focus on the ABCs: airway, breathing and circulation. During the primary survey, if there is any evidence of respiratory distress, oxygen should be administered via mask or flow-by. Because lung sounds are much quieter than in the adult patient, a quiet room is necessary for accurate evaluation of the respiratory system. Mucous membrane colour, capillary refill time (CRT), heart rate, rectal temperature and pulse quality should be evaluated to assess perfusion. Pale mucous membranes and a slow CRT along with poor femoral pulses and cool extremities are supportive of dehydration and hypovolaemia. A normal heart rate does not rule out significant hypovolaemia as the neonatal patient has a limited ability to increase heart rate. As stated previously, dehydration is difficult to assess in the paediatric patient and therefore the veterinary surgeon should assume that any paediatric patient with a history of decreased oral intake is dehydrated. A complete 'tip of the nose to tip of the tail' physical examination should be performed once the patient has been stabilized.

In an unstable patient, an intravenous catheter should be placed for initial blood sampling, intravenous fluid administration and administration of medications (Figure 15.13). A 22–25 G over-the-needle catheter can often be placed in the cephalic or saphenous vein, although a larger catheter may be possible in juvenile patients. A jugular catheter is also an appropriate choice, as long as there is no evidence of a coagulopathy or head injury, and may be easier to place in very small neonates or juvenile patients. In cases where intravenous access cannot be obtained, an intraosseous catheter using a 20–25 G hypodermic needle can be placed for short-term administration of fluids, blood products and medications (Figure 15.14). Normally, an intraosseous catheter is placed in the trochanteric fossa of the proximal femur or the medial aspect of the proximal tibia following aseptic technique (see Chapter 2). Ideally, to minimize infectious complications intravenous access is established as soon as possible in these patients, generally within a few hours of the placement of an intraosseous catheter. Fluids may also be administered subcutaneously and intraperitoneally in paediatric patients; however, intravenous or intraosseous fluid administration is preferred, especially in hypoglycaemic and hypovolaemic patients. Orally administered fluids should be avoided in sick paediatric patients, as decreased gut motility and concurrent gastrointestinal tract disease may decrease the chances of fluid absorption and increase the risk of aspiration.

During establishment of intravenous access, a minimum database (PCV, total solids (TS), blood glucose, dipstick blood urea nitrogen (BUN)) and blood smear (to evaluate white blood cell count, platelet count and red



15.13 Placement of an intravenous catheter in a puppy.



15.14 Intraosseous catheter (22 G hypodermic needle) placed in the femur of a Yorkshire Terrier puppy.

blood cell morphology) should be obtained and requires only a small amount of blood. In larger paediatric patients, blood should also be drawn for a complete blood count and biochemical evaluation at the time of initial catheter placement. It is important to monitor the amount of blood that is collected for sampling purposes during the course of hospitalization, as no more than 10% of the blood volume should be phlebotomized per week. For reference, the normal blood volume is 80–90 ml/kg in the dog and 40–60 ml/kg in the cat.

An important diagnostic consideration when evaluating the minimum database is that paediatric patients have a lower PCV, total protein and BUN than adults. In neonatal puppies, the PCV is 47% at birth but drops to approximately 29% at 28 days. In neonatal kittens, the PCV is approximately 35% at birth and decreases to 27% at 28 days. Therefore, a normal adult PCV in a paediatric patient suggests haemoconcentration secondary to dehydration. Neonates have a decreased total protein due to their immature immune system (less production of globulins), and lower blood albumin and BUN are thought to be secondary to immature liver function.

A hypoglycaemic animal (blood glucose <60 mg/dl or 3.3 mmol/l) with supportive clinical signs should be treated immediately with intravenous dextrose. If blood cannot be obtained during catheter placement for blood glucose measurement, the veterinary surgeon should err on the side of treating presumed hypoglycaemia in a patient with suggestive clinical signs (see above). An intravenous or intraosseous bolus of 0.25–0.5 g/kg of dextrose (or 0.5–1 ml/kg of 50% dextrose) is diluted to <10% with an isotonic crystalloid and administered over 2–5 minutes. Ideally, blood glucose should be checked following the bolus to ensure adequate correction of hypoglycaemia. However, administration of additional boluses of dextrose can be based on the patient's clinical response to treatment (i.e. the patient is more responsive, active, moving around, seizures cease). Intravenous fluids should then be supplemented with 2.5–5% dextrose to prevent recurrence of hypoglycaemia until the animal is eating adequately on its own (food should not be offered until concurrent hypothermia and hypovolaemia have been corrected). Blood glucose should be checked every 2–4 hours to monitor for recurrence of hypoglycaemia, or more often if the animal develops clinical signs consistent with recurrent hypoglycaemia. If the initial dextrose supplementation in the intravenous fluids does not supply adequate glucose to prevent recurrence of hypoglycaemia, then the rate of administration of the intravenous fluids could be increased or a higher concentration of dextrose can be administered. If higher concentrations of dextrose (>5%) need to be given, fluids should be administered through a central line such as a jugular catheter.

A patient that is assessed as hypovolaemic should be given an intravenous (or intraosseus) bolus of *warm* isotonic crystalloids. Lactated Ringer's solution may be the preferred crystalloid in neonates, since lactate is the preferential metabolic fuel in conditions of hypoglycaemia; however, any balanced electrolyte solution is acceptable. An initial fluid bolus of 20–40 ml/kg in a puppy and 10–20 ml/kg in a kitten should be given over 15–20 minutes. Additional boluses of fluid should be based on improvement in vital signs, pulse quality and blood pressure (if it can be assessed accurately). Once hypoperfusion has been corrected, intravenous fluid therapy should be initiated to provide maintenance fluid needs as well as replacement of dehydration and ongoing losses (urinary, respiratory and gastrointestinal tract). Maintenance fluid requirements (80–100 ml/kg/day or 3–4 ml/kg/h) for paediatric patients are higher than for their adult counterparts. This increased daily fluid requirement stems from increased total body water, higher body surface area, decreased body fat (loss of heat), increased metabolic rate, reduced urine concentrating ability and increased insensible losses. The patient should be monitored closely for both under- and overhydration during intravenous fluid therapy. Immature kidneys are unable to dilute urine (in addition to lacking concentrating ability), which increases the risk of fluid overload. Serial measurement of bodyweight on an accurate scale (approximately every 6–8 hours) as well as frequent re-evaluation of vital parameters is used to monitor the animal's response to the fluid therapy.

Treatment and prevention of hypothermia is another important aspect of the stabilization and treatment of the paediatric patient. Body temperatures less than 37.2°C should be treated. Incubators, warm water recirculating blankets, forced warm air blankets (Bair Hugger®), heat lamps and warm towels can all be used to increase the ambient temperature and allow for external warming. The patient should have the ability to move away from the heat source to avoid overheating. In the initial stabilization period, room temperature intravenous fluids should be avoided as this may exacerbate hypothermia. A patient

that is concurrently hypovolaemic should be warmed slowly after being volume resuscitated, to avoid peripheral vasodilatation and worsening hypotension.

Oxygen supplementation should be given to paediatric patients with signs of respiratory distress (see above). Ideally, oxygen is administered via a face mask or oxygen cage, but in animals with severe distress it may be given via endotracheal tube if mechanical ventilation is required. Aiming for an F_iO_2 (fraction of inspired oxygen) of <60% is ideal since paediatric patients are more at risk than adults for the development of retrolental fibroplasia (blindness) associated with the delivery of high concentrations of oxygen for extended periods of time. Objective assessment of the animal's oxygenation status with pulse oximetry and/or arterial blood gas analysis may also be considered to confirm the presence of hypoxaemia and monitor response to treatment (see Chapter 7). Chest radiography can be performed in stable patients to determine the underlying aetiology of the respiratory distress, remembering that the thymus, located in the cranial thorax on the left side, will be present and should not be misinterpreted as a mediastinal mass or lung consolidation.

Once the patient is stabilized, a secondary survey or full physical examination should be performed. In the neonatal patient, careful evaluation of the oropharynx to assess for the presence of a cleft palate, palpation of the fontanelle, and palpation and visual inspection of the umbilical site to assess for infection and the presence of an umbilical hernia should be performed. Gentle abdominal palpation to assess for foreign body obstruction and intussusception should also be performed.

Additional therapies and diagnostic testing (i.e. bloodwork, faecal parasite screening, radiography, ultrasonography) should be directed at the suspected underlying cause of the patient's clinical signs and should only be pursued once the patient is stabilized. Of note, parvovirus testing should be done in any weaned paediatric dog with supportive clinical signs (vomiting and diarrhoea) and an incomplete vaccination history. It is also the authors' practice to routinely administer anthelminthic treatment to paediatric patients with gastrointestinal signs with pyrantel pamoate. In animals that are vomiting, antiemetics such as ondansetron (0.1–0.2 mg/kg i.v. q12h) or maropitant (1 ml/kg i.v. q24h in dogs >8 weeks of age and in cats >16 weeks) should be administered and are generally effective in controlling emesis.

Septicaemia in both neonatal and juvenile animals is common. In addition to respiratory and gastrointestinal tract infections (see above), septicaemia may also result from tail docking and umbilical cord ligation. Neonatal animals are particularly prone to systemic infection due to their poorly developed immune systems and/or inadequate ingestion of colostrum in the postparturient period that is essential for provision of passive immunity. Therefore, empirical antibiotics are typically initiated early during the stabilization period of critically ill paediatric patients to cover for possible sepsis. Beta-lactam antibiotics (i.e. cephalosporins and penicillin derivatives) are a good first-line treatment and are considered safe to use in paediatric patients. However, due to concerns about decreased hepatic clearance, some authors recommend that the dose interval be adjusted to every 12 hours rather than every 8 hours (Boothe and Tannert, 1992). Antibiotics that are generally avoided in neonates include aminoglycosides (renal damage), tetracyclines (skeletal growth abnormalities and staining of the teeth) and fluoroquinolones (destructive lesions in the cartilage of long bones). One study suggests that the use of co-amoxiclav had the greatest survival rate in 517 puppies treated for bacterial infection as compared with ampicillin alone or cephalosporins (Munnich and Kuchenmeister, 2014). It is important to note that antibiotics can contribute to diarrhoea, and the administration of probiotics may be useful in these instances.

Finally, analgesic medication should be given to a paediatric animal with traumatic injuries or in which painful procedures need to be performed. Opioids (fentanyl, morphine, buprenorphine) are a good first choice as they tend to have minimal effects on the cardiovascular or respiratory system; the pure opioids can also be reversed with naloxone should adverse effects be seen. Lower doses of opioids (half of the adult dose is generally recommended) are required for analgesia in the neonatal period compared with older puppies (>4 weeks). It is prudent to start with a low dose and then titrate to effect. The use of NSAID pain medications is not recommended for animals less than 6 weeks of age.

Resuscitation of the neonate

Neonatal mortality rates are reported to be high, ranging from 9 to 26%, and therefore, prudent veterinary intervention in the immediate post-partum period for selected neonates may improve survival (Mila *et al*., 2015). In most cases of an uncomplicated vaginal delivery, and if the neonate is vigorous, vocalizing, and if the dam is appropriately attending to the neonate, veterinary intervention may not be needed. However, if the neonate is not moving or vocalizing, or in cases of prolonged labour, or in neonates delivered via a Caesarean section, veterinary intervention is warranted.

The appropriate resuscitation of a neonate in veterinary medicine should include an evaluation of the ABCs in addition to warming. The neonate should be quickly evaluated (<10 seconds) for the presence of spontaneous ventilatory efforts and vocalizing, and the heart rate should be evaluated. Bradycardia (heart rate <180 bpm), absent or inadequate respiratory efforts, and weak or no crying signals neonatal distress. A modified Apgar score, as developed by Veronesi *et al*, may be calculated by concurrently evaluating the puppies' reflex irritability (gentle compression of the tip of the paw should cause a reaction), motility (spontaneous movements) and mucous membrane colour. Puppies with a low Apgar score are more likely to die and therefore this score may help guide the veterinary surgeon when deciding whether veterinary intervention is indicated.

The neonate should be gently but vigorously dried off with a warm towel to promote respiratory efforts and prevent the development of hypothermia. In a neonate with inadequate ventilatory efforts, an infant nasal aspirator can be used to gently suck any remaining amniotic fluid from the nares and pharynx. This process can also be facilitated by lowering the head below the thorax for passive drainage of amniotic fluid. The authors would strongly caution against the use of 'swinging' the neonate – cradling the puppy in cupped hands with the head stabilized and swinging the neonate in a gentle downward arch from the mid-abdomen height to knee height in an attempt to remove amniotic fluid. Although previously a popular technique for resuscitation in neonatal animals, it is dangerous due to the high risk for intracranial trauma. A recent case of a seizuring neonatal puppy reported that subdural and intracerebral hemorrhages were found at post-mortem examination consistent with high-velocity deceleration trauma from being 'swung' during its initial resuscitation.

Oxygen supplementation to improve hypoxaemia can be provided via either a mask or flow-by during the resuscitation period. In neonates that are still not ventilating adequately, stimulating the Jen Chung acupuncture point (GV 26, location of respiratory neuroreceptors) is a non-invasive method to stimulate ventilatory efforts. In this technique, a small-gauge needle (25 G) or acupuncture needle is inserted into the nasal philtrum at the base of the nares to the level of the cartilage/bone and the needle is rotated and removed. Doxapram, a non-specific central nervous system stimulant, is no longer recommended to stimulate ventilation as it is unlikely to improve hypoxaemia.

In neonates that fail to breathe spontaneously after the above efforts have been instituted, ventilatory support should be initiated. Positive pressure ventilation can be given via a tight-fitting mask or via endotracheal intubation, being careful not to exceed 10 cm H_20 of inspiratory pressure. The chest should be watched to ensure appropriate lung expansion. Reversal of hypoxaemia should improve myocardial function, reversing bradycardia and improving tissue perfusion. If asystole or severe bradycardia is persistent despite ventilatory support, external cardiac compressions can be initiated and delivered at a rate of at least 120 bpm. Intravenous access should be attempted and a skilled phlebotomist may be able to place a small-gauge catheter (24 G) in the cephalic or jugular veins for intravenous administration of medications and fluid therapy. At the time of catheter placement, a blood glucose measurement should be obtained to evaluate for hypoglycaemia (see above for treatment). Alternatively, if intravenous catheter placement is unsuccessful, intraosseous (see Chapter 2) or umbilical vein catheterization may be performed. Once intravenous or intraosseous access has been obtained, adrenaline (0.01 mg/kg i.v. or orally) may be administered for asystole or severe bradycardia. If none of the above techniques to establish intravenous or intraosseous access is possible, adrenaline may be administered sublingually.

During and immediately following the resuscitation period, the prevention of hypothermia is essential. External heat support should be supplied through warm towels, heating lamps or forced air warming devices (Bair Hugger®). The normal body temperature of the neonate during the first 7 days ranges from 35 to 37.2°C and hyperthermia should be avoided. Once the neonate has been adequately resuscitated, the umbilicus should be ligated with suture and treated with a 2% iodine solution to prevent bacterial infection. Ideally, as soon as the neonate has been stabilized, it should be placed back with the dam to allow for adequate intake of colostrum, which can only occur within the first 24 hours following parturition. Kittens that lack an effective suckle may be given 150 ml/kg (or 0.15 ml/g, divided into several doses and administered during the first 24 hours) of adult serum subcutaneously or intraperitoneally to replace oral ingestion of colostrum. The appropriate dose of adult dog serum for puppy colostrum replacement is currently unknown. One study evaluating the administration of 40 ml/kg of adult dog serum to puppies orally and parenterally failed to achieve similar levels of immunoglobulin as in suckling littermates (Bouchard *et al*., 1992).

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Chapter 16

Endocrine emergencies

Barbara J. Skelly

This chapter will cover the following endocrine emergencies:

- Diabetic ketoacidosis
- Insulinoma
- Hypoadrenocorticism
- Hyperaldosteronism
- Hyperadrenocorticism
- Hyperparathyroidism
- Hypoparathyroidism
- Phaeochromocytoma.

Diabetic ketoacidosis

A diabetic ketoacidotic (DKA) crisis can arise in an animal with previously diagnosed diabetes mellitus (DM) or it can be the first indication that either insulin production has fallen or that another disease has developed that causes insulin resistance in the face of reduced insulin production. Once dogs are diagnosed with DM they usually remain insulin-dependent for life, while cats, which usually develop type II DM, may present the further challenge of having waxing and waning insulin requirements.

Figure 16.1 lists the most common reasons for DKA to develop, either in an animal already being treated for DM or in a previously undiagnosed diabetic. Causes are numerous and encompass management changes as well as the presence of concurrent diseases.

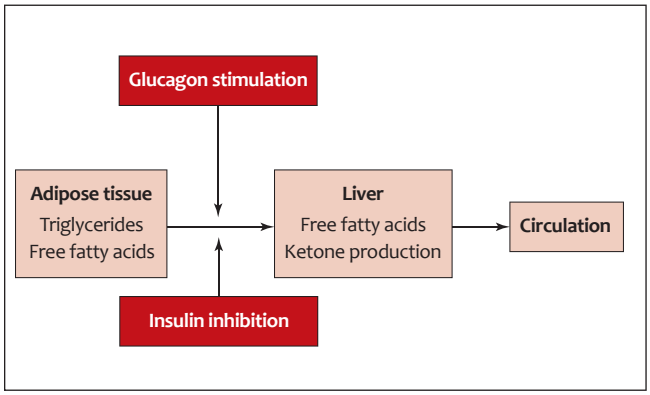
Management-related causes of instability
• Incorrect storage and/or administration of insulin • Short duration of action of insulin • Somogyi overswing • Concurrent steroid therapy (may be topical)
Bacterial infections
• Urinary tract infection • Prostatitis • Pneumonia • Pyoderma • Otitis externa • Any other significant infection
Inflammatory diseases
• Pancreatitis
Endocrinopathies or physiological endocrine changes
Dogs
• Hyperadrenocorticism • Acromegaly (growth hormone from mammary glands) • Hypothyroidism • Phaechromocytoma • Dioestrus phase of oestrous cycle • Glucagonoma
Cats
• Hyperadrenocorticism • Acromegaly (due to pituitary gland tumour) • Hyperthyroidism

16.1 Conditions that can trigger diabetic ketoacidosis (DKA) through insulin resistance.

How does ketoacidosis develop?

DKA develops when the counter-regulatory hormones (chiefly glucagon, but also cortisol, growth hormone and catecholamines) dominate over a reduced or negligible insulin output. Figure 16.2 shows the role of glucagon *versus* insulin in the development of ketoacidosis. Glucagon promotes glycogenolysis and the formation of ketoacids, while a lack of insulin allows free fatty acids (FFA) from the breakdown of adipocyte triglyceride stores to be released into the circulation and taken up by the liver for ketoacid production.

Insulin is also required for metabolism of ketones to carbon dioxide and water. While there is a low level of ketone production in uncomplicated DM, the addition of further physiological stress in the form of an infection, for example, allows ketone production to accelerate and exceed the rate at which ketones can be metabolized. Ketonuria and a metabolic acidosis then develop.



16.2 The effects of insulin and glucagon on lipolysis and ketone production.

BSAVA Manual of Canine and Feline Emergency and Critical Care, third edition. Edited by Lesley G. King† and Amanda Boag. ©BSAVA 2018

Clinical signs

The clinical signs of DKA are listed in Figure 16.3. A detailed history may reveal previous signs of DM, and would be expected to include polyuria and polydipsia, a ravenous appetite and weight loss. Patients in DKA can also develop acute renal failure, so it is useful to know when the animal was last seen to pass urine. Patients are commonly both hypovolaemic and dehydrated on presentation.

- Historical polyuria/polydipsia
- Anorexia and nausea
- Vomiting and/or diarrhoea
- Depression
- Weakness or collapse
- Poor body condition[a]
- Hepatomegaly
- Acetone smell on breath
- Deeper and more rapid respiration reflecting metabolic acidosis (Kussmaul breathing in human medicine)

16.3 Clinical signs of diabetic ketoacidosis (DKA). [a]Some patients that present with DKA precipitated by an acute drop in insulin output or insulin resistance may be of normal bodyweight or obese. Dogs with diabetes mellitus and DKA due to pancreatitis may present like this during an episode of acute pancreatitis.

Diagnosis

DKA is an important differential diagnosis for a collapsed, volume-depleted patient, and early recognition of the disease is vital so that therapy can be initiated quickly. The following is an action plan that could be applied to most collapsed, volume-depleted patients with a view to making the diagnosis as quickly and easily as possible (see also Chapter 1).

Initial patient assessment

- Packed cell volume and total solids.
- Glucose measurement (using point-of-care glucometer).
- Urinalysis:
  - Specific gravity
  - Dipstick analysis – assess for ketones
  - Sediment examination
  - Submit for culture.
- Electrolytes.
- Renal function assessment – urea, creatinine and phosphorus.
- Blood gas analysis (venous is acceptable).

The measurement of a high blood glucose concentration prompts the testing of serum ketone levels. This can be done by clinical pathology laboratories but also by using urine dipsticks with serum or urine as a substrate. In some cases this may require the addition of hydrogen peroxide to oxidize beta-hydroxybutyrate to acetoacetate. In both dogs and cats, but more dramatically in the latter, hyperglycaemia can accompany stress and this may lead to confusion in the diagnosis of DM. This effect is seen most frequently in sick, hypovolaemic cats, which may have blood glucose levels greater than 15 mmol/l. There is no absolute cut-off value to distinguish between stress and true DM but it is rare to have blood glucose values >20 mmol/l due to stress alone. Repeated glucose readings whilst volume replacement is taking place may be required to provide conclusive evidence that the hyperglycaemia is a non-stress-related finding.

Management

Initial management of DKA involves correcting the intravascular volume, hydration and electrolyte abnormalities whilst providing insulin to reduce hyperglycaemia and promote ketone metabolism. The amount of volume replacement depends on the clinical assessment of the degree of hypovolaemia in a particular patient.

- Place a jugular or peripheral vein catheter of the widest bore possible. The benefit of a jugular catheter is that it allows frequent blood sampling without the need for repeated venepuncture. However, longer, thinner catheters present more resistance to fluid flow, so a shorter, peripheral catheter is usually a better option if shock boluses of fluids are needed.
- Begin fluid therapy using an isotonic replacement fluid, e.g. 0.9% NaCl or Hartmann's solution. The latter may be beneficial in cases where the blood pH is extremely acidic as 0.9% NaCl may, in some circumstances, contribute to acidosis through a dilutional effect.
- If the patient is in shock or acute renal failure, use fluid boluses to improve pulse quality and initiate urine output. Fractions of shock doses (incremental doses of 25–30% of the total shock dose of 50–90 ml/kg in the dog and 20–50 ml/kg in the cat; for example, a dog might receive up to four boluses of 20 ml/kg, each over about 15–20 minutes) can be used to effect, with careful monitoring between boluses.
- Once the patient's cardiovascular status has improved, fluid boluses are discontinued and a longer term fluid rate (ml/kg/h) rate is initiated. This rate is initially an estimate based on the degree of dehydration that needs replacing and the animal's ongoing maintenance requirements and losses. As ongoing polyuria caused by osmotic diuresis can be dramatic, fluid rates must be maintained at or above the rate of urine output in the patient. The aim is to correct the hydration and metabolic abnormalities slowly over 24–48 hours so that complications are avoided. Problems that may be encountered include:
  - Hypokalaemia
  - Hypophosphataemia
  - Cerebral oedema.
- Intravenous antibiotics may be started after urine and/or other culture samples have been taken, because of the strong association between bacterial infection and the precipitation of DKA. Ampicillin (20 mg/kg i.v. q6–8h) is a good broad-spectrum choice to use until cultures or other diagnostic tests provide information to allow tailoring of treatment to the specific bacteria involved. If there is evidence of sepsis, the antibiotic spectrum often needs to be broadened to include better Gram-negative coverage.

Monitoring potassium

Although many DKA patients have a whole-body potassium deficit, the plasma potassium concentration may be disarmingly normal at initial assessment. This occurs because of the effect of solvent drag, whereby high extracellular glucose levels encourage the movement of water and potassium out of the cells. When fluid replacement and insulin therapy occurs, however, potassium again takes up an intracellular location and hypokalaemia results.

Severe hypokalaemia can lead to muscle weakness and can predispose to cardiac arrhythmias. It is important to monitor potassium levels every 1–2 hours, especially during the first 12 hours of therapy, and to supplement

the fluids with potassium as appropriate (Figure 16.4). Potassium supplementation as outlined in Figure 16.4 is appropriate for intravenous fluids being administered at maintenance rates only.

If fluid replacement and potassium replacement are being delivered through the same intravenous catheter then the fluid rate needs to be taken into account when the potassium supplementation is calculated. For example, an animal with a potassium of 2.7 mmol/l would need 40 mmol of potassium added to the fluid bag if running at 2 ml/kg/h but would only need 20 mmol of potassium if running at 4 ml/kg/h. The maximum recommended rate of intravenous potassium administration is 0.5 mmol/kg/h and the rate actually being used should be calculated in each case.

Serum potassium (mmol/l)	Amount of potassium to add to 1 l fluids/mmol
>5.5	None – reassess later
4.1–5.4	20
3.1–4.0	30
2.6–3.0	40
<2.5	60–80

16.4 Potassium supplementation of intravenous fluids in patients with diabetic ketoacidosis. The quantities recommended in this chart refer to fluids administered at maintenance rates only (2 ml/kg/h). If higher fluid rates are used, the number of mmol of potassium added must be decreased proportionately so that the rate of administration of potassium does not exceed 0.5 mmol/kg/h.

Monitoring magnesium

Magnesium is an essential co-factor of the sodium/potassium ATPase pump and, although not proven in dogs (Fincham *et al*., 2004), hypomagnesaemia can contribute to poor success rates in the correction of hypokalaemia. Magnesium supplementation may therefore be required in a diabetic animal that has hypokalaemia that is not responding to supplementation. A dose of 0.5–1 mmol/kg/day as a continuous intravenous infusion of magnesium sulphate is commonly used. Oral magnesium supplementation can lead to diarrhoea.

Monitoring phosphate

Total body phosphate may also be depleted, despite being within the normal measured range at presentation (Willard *et al*., 1987). Severe hypophosphataemia may develop on the second day of therapy when phosphate translocates to the intracellular compartment under the influence of insulin. Severe hypophosphataemia may lead to haemolytic anaemia (see Chapter 13). Phosphate should therefore be monitored every 6 hours over the first 2–3 days of treatment. Phosphate supplementation (potassium phosphate 0.01–0.09 mmol/kg/h for 4–6 hours) is recommended if the phosphate concentration drops below 0.35 mmol/l. At the end of this period phosphate should be re-measured and the dose adjusted. At the higher phosphate supplementation doses, close monitoring is essential to avoid hyperphosphataemia. As it is typically administered as potassium phosphate, the additional potassium supplementation should be taken into account and the dose factored in to the total amount of potassium that the animal is receiving.

Neurological function

During prolonged hyperglycaemia, the central nervous system (CNS) protects itself from dehydration by the generation of idiogenic osmoles that help to retain water within the intracellular space. If rehydration or insulin administration occurs too rapidly, resulting in a drop of blood glucose faster than the intracellular idiogenic osmoles can be metabolized or removed, then water will move into neurons and cause oedema. This can lead to worsening neurological function in the early stages of therapy and is an indication that blood glucose has decreased too quickly.

Insulin therapy

Insulin therapy is the cornerstone of treatment as it allows glucose to be taken up by cells for metabolism and prevents further lipolysis from adding to the ketone burden. It also promotes metabolism of ketones. Hence, as serum glucose levels reduce, paradoxically, glucose may need to be added to the intravenous fluids to allow continued insulin administration until the resolution of ketosis. Neutral (soluble) insulin should be used as it facilitates accurate control of glucose levels. Insulin can be given in two ways.

Method 1 (intramuscular):

- Begin treatment with a 0.2 IU/kg i.m. bolus of neutral (soluble) insulin.
- Repeat intramuscular injections of 0.1 IU/kg hourly according to blood glucose measurements to keep blood glucose in the 8–15 mmol/l range.
- If blood glucose drops to <8 mmol/l, add 5% dextrose to intravenous fluids.
- Use neutral insulin for the initial therapy or until the animal begins to eat reliably. At this point, maintenance stabilization using the chosen long-term insulin, e.g. lente, NPH or glargine, can begin.

Method 2 (intravenous constant rate infusion):

- Mix 25 IU neutral (soluble) insulin with 500 ml 0.9% sodium chloride to make a solution of 0.05 IU/ml.
- Deliver insulin at a rate of 1–2 ml/kg/h (0.05–0.1 IU/kg/h). It is easiest to use a separate syringe driver/burette to delivery. This infusion can be run alongside the main fluid source, which can then be adjusted as the patient requires without altering the rate of insulin delivery.
- Insulin solutions within a burette should be protected from direct light by covering with aluminium foil and should be freshly made up at least once every 24 hours.
- Since insulin binds to plastic tubing in drip lines, allow fluids to run through and discard the fluid until a stable solution has been achieved (30–50 ml expelled).
- Blood glucose needs to be checked after 1 hour and then every 1–2 hours thereafter.
- If hypoglycaemia occurs, dextrose can be used as required to maintain the blood glucose at between 8 and 15 mmol/l.
- Longer-acting insulin (e.g. lente, NPH, glargine) can be introduced as above when the animal starts to eat.

If a good response is achieved after the first 24 hours then the intensity of the monitoring can be reduced and the animal tapered off intravenous fluids gradually as it begins to drink and eat. After the first 24 hour period it may be necessary to change the type of fluids depending on the plasma sodium concentration, such that if sodium is >145 mmol/l then a change to Hartmann's solution or 0.45% saline would be advantageous.

Insulinoma

Insulinomas are classically described in middle-aged and older, overweight large-breed dogs and have also been reported rarely in cats (Kraje, 2003). Over-production of insulin induces a profound hypoglycaemia, particularly in a fasted animal. Some clinical signs are also attributed to the increased activity of the sympathetic nervous system and excessive adrenaline (epinephrine) release. The aetiology of an insulinoma-associated polyneuropathy is not certain and may involve axonal degeneration due to hypoglycaemia and/or immune-mediated mechanisms (Van Ham *et al*., 1997). The differential diagnosis of hypoglycaemia is shown in Figure 16.5.

Endocrine
• Insulinoma • Hypoadrenocorticism
Hepatic insufficiency
Neoplasia
• Hepatoma • Hepatocellular carcinoma • Leiomyosarcoma • Insulinoma
Sepsis/systemic inflammatory response syndrome
Patient factors
• Juvenile (toy breed) hypoglycaemia • Hunting dog hypoglycaemia • Neonatal hypoglycaemia
Laboratory error
• Polycythaemia • Aged sample
Iatrogenic
• Insulin overdose • Oral hypoglycaemic agents
Toxic
• Xylitol ingestion (dog)

16.5 Differential diagnosis of hypoglycaemia.

Clinical signs

The history usually involves collapse at exercise or exercise intolerance, weakness, tremors and neurological signs including, more rarely, signs of a polyneuropathy that may present as hindlimb weakness, tetra- or monoparesis. Occasionally animals may present with seizures or blindness. The clinical signs are rapidly responsive to feeding and can be controlled by feeding regular small meals.

Diagnosis

Clinical pathology

The hallmark of insulinoma is the measurement of low serum glucose concentrations with concurrently high levels of insulin. Insulin may not be outside the normal range (5.0–20 IU/ml) but may be inappropriately high for the blood glucose. If insulinoma is suspected but the blood glucose is in the normal range then supervised fasting of the animal can be conducted with glucose measurements every 2–3 hours. Hypoglycaemia will usually result in 6–8 hours if an insulinoma is present. Insulin:glucose and amended insulin:glucose ratios do not contribute to the ease of diagnosis and are not used by this author. The measurement of a low fructosamine whilst albumin is normal (normal range 258–343 μmol/l) can add to the index of suspicion. Glucagon tolerance tests are rarely necessary although they may be used in cases with results that are difficult to interpret. There are no other consistent abnormalities on clinical pathology measurements.

Imaging

Radiographs are unlikely to yield diagnostic information but abdominal ultrasound examination is useful in the identification of pancreatic nodules and also to assess other abdominal organs, particularly the liver, for abnormalities that suggest metastasis.

Confirming a diagnosis

Ultimately, a definitive diagnosis is reached if an exploratory laparotomy identifies a pancreatic lesion that may be evaluated by histopathology.

Treatment

Emergency treatment

Patients with neurological signs caused by hypoglycaemia need immediate attention. After collecting blood for glucose and insulin assessment, dextrose should be given as a bolus (10% dextrose solution at 0.2 g/kg i.v. (0.2 ml/kg)). The clinical response is usually rapid and stability should then be maintained by the addition of 2.5–10% dextrose to intravenous fluids. If the dextrose concentration is >5% then a central route of administration should be used to avoid thrombophlebitis caused by administration of a hypertonic solution through a peripheral vein. If a central line is not available, dextrose supplementation can be maintained at 5%, and a higher absolute amount of dextrose can be administered by increasing the fluid rate.

The use of a glucagon infusion (5–40 ng/kg/min i.v. diluted in saline) has been reported in a case of insulinoma in a dog that was refractory to dextrose treatment (Fischer *et al*., 2000). Glucagon was found to induce normal blood glucose for a period of 3 weeks, presumably through the mechanism of insulin resistance.

Longer-term medical management

- Successful medical management involves multiple feeds per day using foods of low glycaemic index.
- Prednisolone (0.2–0.5 mg/kg q12–24h) is also frequently used to induce insulin resistance and is cheap and easily available.
- Diazoxide, a benzothiazide diuretic that inhibits insulin release via stimulation of alpha-adrenergic receptors, can help to maintain euglycaemia in dogs in which prednisolone side effects become dose limiting. Side effects of diazoxide include nausea and sodium retention that may lead to oedema. The dose rate of diazoxide is 10–30 mg/kg/day, which is usually administered in three divided doses. (This drug is not licensed for use in cats or dogs in the UK.)
- Octreotide is a somatostatin analogue that may be of benefit in refractory cases. It also has the potential to worsen clinical signs in that
  it may lower glucagon and growth hormone concentrations. It is available as an injectable preparation only, so is not suitable for use in every case. (This drug is not licensed for use in cats or dogs in the UK.)

Surgical management

Surgery may be useful in the management of insulinoma in that it may help to confirm a diagnosis and, if removal of a solitary nodule is possible, may allow for a disease-free interval during which no medication is necessary. Out of 285 reported cases, 129 (45%) were found to have evidence of metastatic disease at the time of surgery (de Brito Galvao and Chew, 2011). No respite from clinical signs would therefore be expected in this group. In this author's experience there seems to be a clinical spectrum within the diagnosis of insulinoma whereby occasional animals have appropriate clinical signs, low glucose concentrations in the face of elevated insulin and confirmatory histopathology, but become completely disease-free after surgical removal of a pancreatic nodule. These insulinomas behave in a benign way and have little metastatic potential. Other animals, however, have extremely aggressive tumours and even after surgical excision, gain only a short respite from hypoglycaemia and associated clinical signs. Despite this, median survival in surgically managed dogs (with or without medical management) is far greater (436 days) than median survival in dogs that receive only medical management (124 days; Tobin *et al*., 1999; Polyon *et al*., 2007).

Other factors to be taken into consideration include the possibility that manipulation of the pancreas during surgery can precipitate acute pancreatitis, and that removal or damage to the pancreas can result in DM or exocrine pancreatic insufficiency.

Chemotherapy

Streptozotocin is an alkylating agent whose use has been reported in insulinoma. It has been shown to be beneficial in some cases but nephrotoxicity is a limiting factor (Moore *et al*., 2002).

Hypoadrenocorticism

Hypoadrenocorticism (Addison's disease) is usually caused by immune-mediated destruction of the adrenal cortex leading to a reduction in the output of the steroid hormones cortisol and aldosterone. This disease occurs in dogs (predominantly young to middle-aged females) and much less frequently in cats. Although a hypoadrenal crisis may occur acutely and deterioration may be rapid, vague, waxing and waning clinical signs have usually been present over a longer period of time. The clinical signs include gastrointestinal signs (anorexia, vomiting and diarrhoea), weight loss, muscle weakness and lethargy. Previous biochemical analysis frequently identifies an intermittent azotaemia and mild electrolyte abnormalities. Some animals only have cortisol deficiency at the time of presentation, but can go on to develop aldosterone deficiency as well.

Why are adrenal steroid hormones important?

Cortisol and aldosterone have vital roles in the mainenance of many different body systems but particularly the gastrointestinal tract, and in renal function and water homeostasis. The gastrointestinal manifestations of hypoadrenocorticism (vomiting and diarrhoea), caused by cortisol deficiency, are signs of a motility disorder. Regurgitation due to poor oesophageal motility and/or megaoesophagus can also be present. Aldosterone mediates the uptake of sodium and loss of potassium in the distal convoluted tubule, so aldosterone deficiency allows excessive sodium loss and therefore water loss through the kidneys, and leads to volume depletion. At the same time, the ability to excrete potassium decreases and hyperkalaemia develops.

Clinical signs

An animal presenting in a hypoadrenal crisis is collapsed, hypovolaemic (as evidenced by poor pulse quality, pale mucous membranes and prolonged capillary refill time) and bradycardic. The latter is one of the signs that may alert the clinician to the diagnosis, as hypovolaemia is usually accompanied by tachycardia. Vomiting, diarrhoea and weight loss are also common and may be reported historically. Animals frequently have a history of polyuria and polydipsia.

Diagnosis

Haematology

A compete blood count is often relatively unremarkable, although there may be mild to moderate anaemia. This is interpreted as anaemia of chronic disease, although it may be severe if there is significant gastrointestinal blood loss. An interesting finding is that there is no stress leucogram (lack of neutrophilia, lymphopenia, eosinopenia), due to the lack of cortisol up-regulation.

Biochemistry

Hyperkalaemia, hyponatraemia, hypochloraemia and hypercalcaemia may all be present when aldosterone is deficient. Animals may be hypoglycaemic due to the lack of insulin antagonism by cortisol. Azotaemia can be mild to severe and may confuse the diagnosis with one of acute renal failure.

Urinalysis

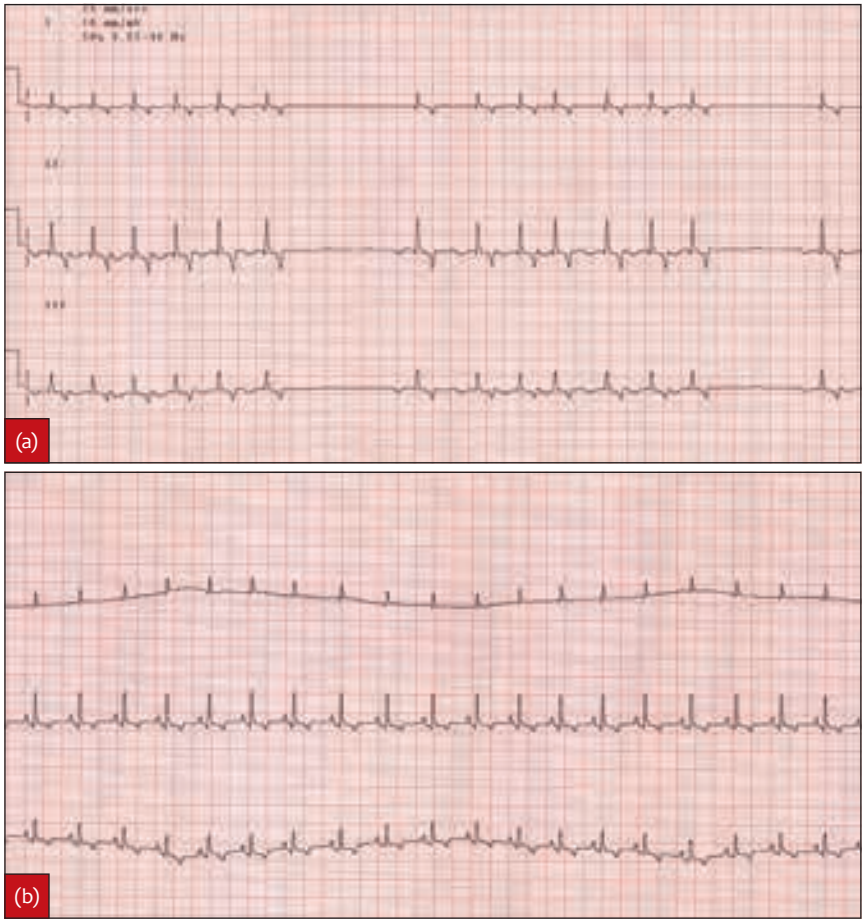
Urine is usually isosthenuric to mildly concentrated (<1.025). This lack of concentrating ability does not usually reflect irreversible renal damage, but merely emphasizes the need for aldosterone in the production of concentrated urine. Hypoadrenocorticism is an important differential diagnosis for young to middle-aged dogs with apparent renal disease defined by azotaemia and isosthenuria; however, the azotaemia of hypoadrenocorticism is commonly prerenal in origin.

Electrocardiography

Electrocardiography may be helpful in determining the nature of the bradycardia noted in most animals with typical hypoadrenocorticism. The rising potassium concentration leads to a blunting of the excitability of conductive tissue in the heart and to a slowing of pacemaker activity. Initially, the P wave becomes depressed and disappears (Figure 16.6), but eventually ventricular activity is also suppressed. Classically, a spiked T wave is described when there is hyperkalaemia, but this is a relatively uncommon sign and is less easy to interpret than the disappearance of the P wave.

ACTH stimulation test

An adrenocorticotropic hormone (ACTH) stimulation test is definitive for hypoadrenocorticism. After the measurement



16.6 (a) An electrocardiogram from a dog with hypoadrenocorticism. The potassium was measured as 8.9 mmol/l at the time of the recording. Atrial activity is suppressed, T waves are larger and peaked, and there are periods of arrest. (b) After emergency treatment the potassium had decreased to 6.4 mmol/l. P waves are now visible, the heart rate has increased and the T wave is much smaller. (Courtesy of N Bexfield)

of basal serum cortisol levels, synthetic ACTH is given intravenously and a post-ACTH sample is taken 30 minutes to 1 hour later. A classical hypoadrenocorticoid picture would show both a low basal cortisol and no measurable stimulation post-ACTH (<20 nmol/l pre- and <20 nmol/l post-ACTH). The ACTH stimulation test can be performed during the initial stages of volume expansion. The administration of dexamethasone does not interfere with this test, although frequently the test can be completed before any steroids are given.

Measurement of basal serum cortisol only may also be used as a screening test for hypoadrenocorticism in dogs. Bovens *et al*. (2014) showed that the disease is unlikely with a basal serum cortisol >55 nmol/l, whereas an ACTH stimulation test is required when serum basal cortisol was ≤55 nmol/l.

Treatment

Emergency treatment

Collapsed, bradycardic and hypovolaemic animals need rapid attention. Urgent volume expansion is required but specific measures may also be necessary to reduce the effects of the hyperkalaemia.

- Begin intravenous fluid therapy using 0.9% NaCl at shock doses (up to 90 ml/kg bolus in dogs, 40–50 ml/kg bolus in cats). Administering the total bolus volume in smaller fractions (increments of 25–30% of the total) with close monitoring is preferable, allowing slowing of the fluid rate once adequate volume expansion is achieved, thus reducing the risk of volume overload. Hartmann's solution may also be used; although it does contain some potassium (5 mmol/l) the positive dilutional effects outweigh the impact of the small amount of potassium that is present.
- In animals with severe hyponatraemia (<125 mmol/l), rapid increases in serum sodium should be avoided or central nervous system signs can result (see Chapter 5).
- Injectable steroids such as dexamethasone sodium phosphate (0.3–1 mg/kg) or prednisolone sodium succinate (0.5–1 mg/kg) can be given and these often improve demeanour. Neither of these drugs has a significant mineralocorticoid effect, however, so they must be followed up with a drug providing this, for example, fludrocortisone (0.1–0.5 mg/kg orally) or desoxycortone pivalate (2.2 mg/kg s.c.). Once a mineralocorticoid replacement has been given, fluids and electrolytes must be monitored carefully to avoid raising the sodium too rapidly or by too much. An alternative to this approach is to use hydrocortisone sodium succinate or phosphate at a dose rate of 0.5–0.625 mg/kg/h as an intravenous infusion. This drug has the benefit of having both glucocorticoid and mineralocorticoid activity. The rate of sodium retention must be monitored closely when using high fluid rates in combination with mineralocorticoid supplementation, as overzealous correction of hyponatraemia should be avoided.

Treatment of severe hyperkalaemic bradycardia

The level of hyperkalaemia that leads to significant cardiac effects varies between animals, but serum potassium levels >7.5 mmol/l are usually associated with impaired

cardiac output. In patients where bradycardia is <30–40 bpm and which do not respond rapidly to volume replacement, more aggressive treatment to reduce hyperkalaemia, or protect the heart from its effects, is warranted. Options for treatment include:

- 10% calcium gluconate (0.5–1.5 ml/kg) given as a slow intravenous infusion with electrocardiographic monitoring. This does not reduce serum potassium levels but instead raises the cardiac threshold potential, re-establishing the difference between the resting and threshold potentials. This is the preferred option for immediate management of life-threatening bradycardia
- Neutral (soluble) insulin (0.2–0.5 IU/kg i.v.) in combination with 2 g of dextrose for every IU of insulin, *or* dextrose by itself, which stimulates endogenous insulin release. This will encourage the redistribution of potassium into an intracellular location and thus rapidly lower, the potassium level. Caution must be exercised to monitor the blood glucose frequently after insulin administration to avoid iatrogenic hypoglycaemia
- Sodium bicarbonate (1–2 mmol/kg i.v.) will also prompt potassium to move into cells. Treatment with sodium bicarbonate is rarely indicated and should only be used if monitoring of acid–base parameters is possible and other treatments have proved unsuccessful.

Other treatment considerations

In animals with gastrointestinal haemorrhage or severe hypoproteinaemia, there may be a requirement for replacement of volume using blood products or whole blood, or for synthetic colloid solutions. Some hypoproteinaemic animals are not able to tolerate large volumes of crystalloids because of their tendency to leak fluid out of the vasculature into body cavities and interstitial spaces. Colloids may be used in these patients; however, their use is controversial and problems with availability limit their use currently (see Chapter 4).

Chronic therapy

Once an acute crisis has been managed, chronic therapy depends on long-term mineralocorticoid replacement therapy (desoxycortone pivalate or fludrocortisone) with or without prednisolone at physiological replacement rates (0.2–0.3 mg/kg/day).

Hyperaldosteronism

Primary hyperaldosteronism (called Conn's syndrome in humans) is characterized by excessive secretion of mineralocorticoids (primarily aldosterone) from an adrenal tumour. Autonomous secretion of aldosterone leads to hypokalaemia and systemic arterial hypertension. It is reported rarely in dogs but is believed to be much more common in cats and may be the most frequent adrenocortical disorder in this species (Djajadiningrat-Laanen *et al*., 2011).

Clinical signs

Muscle weakness occurs when there is moderate to severe hypokalaemia (<2.5 mmol/l), leading to characteristic cervical ventroflexion and a plantigrade stance or general collapse. Systemic arterial hypertension can result in ocular signs including intraocular haemorrhage, hyphaema and retinal detachment. Many cats will present with non-specific signs such as anorexia, depression and weight loss. Skin fragility can be present, particularly if the adrenal mass also secretes progesterone.

Diagnosis

Routine blood-work will usually reveal hypokalaemia but no other consistent abnormalities. Hypernatraemia appears to be an unusual finding (Djajadiningrat-Laanen *et al*., 2011).

Plasma aldosterone is elevated while plasma renin is low, indicating autonomous aldosterone secretion that is not occurring in response to hypovolaemia. The aldosterone:renin ratio can be used diagnostically, but plasma for renin measurement needs to be chilled, separated quickly and frozen to avoid sample renin degradation.

Abdominal radiographs may reveal an adrenal mass, while ultrasound examination can confirm the size and position of the mass.

Treatment

Emergency treatment

Interim treatment is warranted when hypokalaemia is causing clinical signs of collapse and weakness and to control hypertension. Spironolactone (2 mg/kg orally q12h) may be used together with oral or intravenous potassium supplementation (see Figure 16.4). Amlodipine (0.1 mg/kg orally q24h) is most frequently used to control hypertension.

Longer-term management

Adrenalectomy is the treatment of choice as long as only one adrenal is affected. Post-adrenalectomy, food may be supplemented with salt or fludrocortisone may be required to control a relative hypoaldosteronism caused by suppression of the contralateral adrenal gland.

Hyperadrenocorticism

Hyperadrenocorticism (HAC, Cushing's disease) is a chronic disease that is mainly diagnosed after the routine investigation of polyuria/polydipsia in an older dog. HAC may be of pituitary or adrenal origin, although pituitary tumours cause the majority of causes. There are some more critical manifestations of this disease, however, and these will be discussed here.

Pulmonary thromboembolism

Pulmonary thromboembolic disease can cause acute dyspnoea and death in animals with HAC. A pro-thrombotic state is created through the dysregulation of procoagulation *versus* anticoagulation mechanisms; for example, an excess of cortisol can lead to proteinuria and loss of antithrombin through the kidney secondary to the development of glomerular hypertension. Obesity, systemic hypertension, an elevated haematocrit, and concurrent diseases such as hypothyroidism or DM are also predisposing factors.

Diagnosis

Radiographs may be unremarkable, may show areas of increased radiolucency representing areas where pulmonary perfusion has decreased markedly, or may have

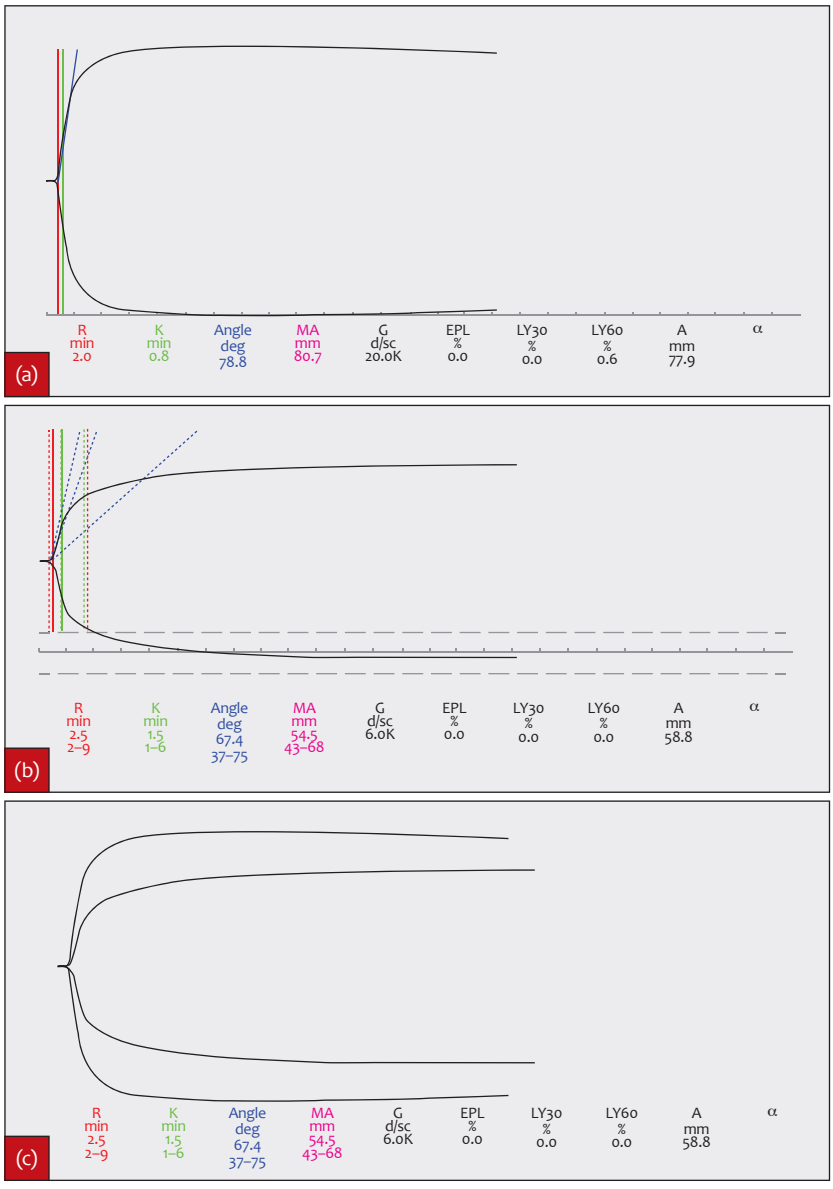
regional or generalized pulmonary infiltrates (alveolar or mixed alveolar/interstitial patterns). Infiltrates may delineate a wedge shape, representing an area of haemorrhage, atelectasis or infarction. Figure 16.7 shows a radiograph from a dog with suspected pulmonary thromboembolic disease affecting the right caudal pulmonary artery. Computed tomography, magnetic resonance imaging and selective pulmonary angiography may help to provide an absolute diagnosis, but as these tests are all carried out under anaesthesia and the patient is often too unstable to anaesthetize, diagnosis is frequently by exclusion (Goggs *et al*., 2009).

Arterial blood gas analysis usually shows hypoxaemia and often hypocapnia secondary to hyperventilation. The alveolar–arterial oxygen gradient is increased.

A coagulation profile is usually not of great help, although D-dimers may be elevated and indicate increased clot turnover. More recently, the use of thromboelastography (TEG) has increased the recognition of when an animal is in a hypercoagulable state (Figure 16.8). However, the documentation of hypercoagulability by TEG simply identifies risk; it does not define whether or not thrombosis has already occurred.



16.7 Dorsoventral thoracic radiograph from a dog with acute-onset dyspnoea. The radiograph shows hyperlucency of the lung fields on the right side. The right caudal lobe pulmonary artery extends to the 11th intercostal space and is of increased diameter with a club-shaped appearance to its terminal aspect. There is also an alveolar pattern in the left cranial lung lobe, which may represent an additional area of pulmonary thromboembolism or a different disease process such as aspiration pneumonia.



16.8 (a) Thromboelastography (TEG) tracing from a dog in a hypercoagulable state. (b) Tracing from a normal dog for comparison. (c) The two TEG tracings shown in (a) and (b) overlying each other to highlight the differences.
(Graphs from TEG 5000 thromboelastograph haemostasis system)

Treatment

Oxygen therapy is used to correct hypoxaemia and to improve cardiopulmonary function. Most thrombi will be broken down spontaneously and patients will improve if they can be supported adequately during this time. Anticoagulant and antiplatelet drugs may be given to reduce the chance of further thrombi being formed. The management of pulmonary thromboembolism is discussed in Chapters 7 and 13.

Thromboembolism in other organs

Portal vein thrombosis (PVT) has also been reported as a potentially life-threatening complication of HAC. Two of the 33 dogs in one report of PVT patients had HAC (Repass *et al*., 2012). Clinical signs included abdominal pain, ascites, thrombocytopenia and shock; systemic inflammatory response syndrome and disseminated intravascular coagulation are possible complicating factors. The use of antithrombotic therapy correlated with survival.

Diabetes mellitus

There is an increased risk of DM in animals with HAC, particularly cats. HAC may contribute to insulin resistance in dogs and cats and may increase the risk of DKA. The treatment of both diseases together is challenging and it is advisable to try to establish diabetic stability before adding a drug to address HAC.

Neurological manifestations

In a proportion of dogs with pituitary tumours (10–15%) the tumour is a macroadenoma rather than a microadenoma, and is therefore more likely to cause neurological signs. For some of these dogs, the treatment of HAC using either trilostane or mitotane will allow a sudden increase in tumour growth or an increase in peri-tumour inflammation due to the reduction in circulating steroids that may have previously been restricting tumour growth by negative feedback. Whilst decreasing the dose of trilostane or mitotane may cause an improvement, the only other method that has been used to reduce the mass effect of the tumour is radiotherapy, which is quite effective (Theon and Feldman, 1998).

Pancreatitis

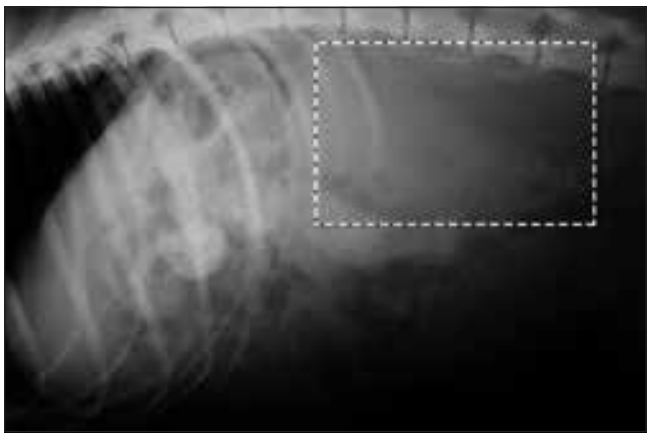
HAC predisposes to acute pancreatitis through a variety of mechanisms (Hess *et al*., 1999). HAC patients are often lipaemic and hypercholesterolaemic as well as being polyphagic. Pancreatic duct hyperplasia and inspissated pancreatic secretions have also been reported. The management of acute pancreatitis is addressed in Chapter 11.

Hypertension

HAC frequently leads to hypertension through cortisol-induced renin secretion. Hypertension can cause ocular signs (intraocular haemorrhage, retinal detachment), neurological signs (depression, signs of headache, specific localizable signs reflecting areas of haemorrhage), glomerular disease and thromboembolic disease. Hypertension is controlled by addressing the primary underlying disease, HAC, and may require specific treatment with antihypertensive drugs, as well as supportive therapy of associated clinical signs.

Adrenal tumour haemorrhage

A rare consequence of the presence of an adrenal tumour is haemorrhage due to tumour rupture (Figure 16.9).



16.9 Lateral abdominal radiograph from a dog showing retroperitoneal haemorrhage due to rupture of an adrenal mass. The image shows dramatic enlargement and streaking of the retroperitoneal space (boxed) with effacement of the kidneys. (Courtesy of A Holloway)

Hyperparathyroidism

Primary hyperparathyroidism can lead to dramatic elevations in blood calcium concentrations through oversecretion of parathyroid hormone (PTH). This disease occurs in dogs of any breed, although Keeshonds have a familial form of the disease and form a significant proportion of total hospital admissions for this endocrinopathy (Refsal *et al*., 2001) (Figure 16.10). The disease is rare in cats (Kallet *et al*., 1991) but may be recognized more easily now that an assay for feline parathyroid hormone is available.

Clinical signs

The clinical signs of hyperparathyroidism include polyuria, polydipsia, muscle tremors, dental pain and bone pain. As serum calcium increases slowly over months, the onset of clinical signs can be insidious and may not be noticed by the owner. Hypercalcaemia causes polyuria through its action on antidiuretic hormone receptors in the renal tubule, which results in nephrogenic diabetes insipidus.



16.10 A Keeshond recovering from surgery to remove a parathyroid nodule.

The kidneys are also vulnerable to damage via the mineralization of renal tubular cells that occurs when there is prolonged hypercalcaemia. A proportion of dogs with primary hyperparathyroidism will present in renal failure, posing a diagnostic dilemma in deciding whether hyperparathyroidism is a secondary or a primary disease. These dogs may have vomiting, diarrhoea, anorexia, depression and halitosis in addition to signs of hypercalcaemia (Gear *et al*., 2005).

Diagnosis

Diagnosis depends on demonstrating hypercalcaemia (both total and ionized) with elevated or inappropriately high PTH and no other cause for the hypercalcaemia. Usually, renal failure causes an increase in total but not ionized calcium, but this is not an infallible rule. In addition, comparison of the degree of azotaemia and the degree of hypercalcaemia can give an indication as to which is the primary problem. Phosphate concentrations are a more reliable distinguishing feature, as they will be elevated in cases of renal failure but suppressed in primary hyperparathyroidism uncomplicated by renal insufficiency.

Imaging

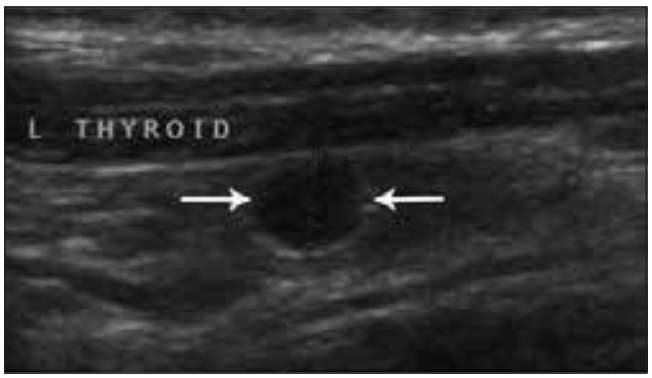
It is usually possible to image the abnormal parathyroid gland in the neck (Figure 16.11). Some dogs may have enlargement of more than one gland.

Treatment

Hypercalcaemia should be dealt with rapidly to avoid precipitating renal failure in dogs with normal renal function. Although some dogs survive for years without treatment and with no impairment of renal function in the face of severe hypercalcaemia (total calcium >3.8 mmol/l), the degree of renal damage already sustained and the likelihood of future development of renal failure is impossible to gauge, and all dogs where treatment is delayed are at risk of developing renal insufficiency. For this reason, severe hypercalcaemia should be treated as a medical emergency.

Fluid therapy

0.9% NaCl is the fluid of choice to induce diuresis and promote calciuresis. Once volume losses have been replaced this can be used in conjunction with furosemide (2–4 mg/kg twice daily) to further increase the excretion of calcium.



16.11 Ultrasound examination of the ventral neck usually reveals a parathyroid nodule, appearing as an echolucent mass (arrowed) within thyroid tissue.
(Courtesy of A Holloway)

Bisphosphonates

Bisphosphonates may be useful in cases of severe hypercalcaemia when the enlarged parathyroid gland cannot be visualized or when there is a delay to treatment. They act to slow bone resorption through the inhibition of osteoclastic activity. Clodronate (10–30 mg/kg orally q8–12h) and pamidronate (1.3–2.0 mg/kg in 150 ml 0.9% saline i.v. delivered over 2 hours) are probably the most frequently used in veterinary medicine.

Surgical management

The most frequent treatment for a parathyroid adenoma or parathyroid tissue hypertrophy is surgical removal. This is made easier if a mass has already been identified ultrasonographically, but surgical exploration of the neck is warranted in any dog with a diagnosis of primary hyperparathyroidism whether or not a parathyroid nodule has been identified.

Other methods

Chemical ablation using ultrasound-directed injection of ethanol has been described (Long *et al*., 1999). The success of this technique is user dependent and, of course, depends on the reliable identification of abnormal parathyroid tissue. Percutaneous ultrasound-guided heat ablation has also been described, although this technique is not offered in many locations (Rasor *et al*., 2007).

Hypoparathyroidism

Primary hypoparathyroidism is a rare condition in dogs and there are few reports in cats (Barber, 2004). The disease occurs secondary to destruction of parathyroid tissue, probably through immune-mediated attack, and the consequent decline in parathyroid hormone production. This leads to a fall in plasma calcium levels to the point where clinical signs of hypocalcaemia are seen. Secondary hypoparathyroidism may occur in cats as a complication of bilateral thyroidectomy.

Clinical signs

The main signs are those of neuromuscular excitability. Affected animals may have facial twitching progressing to generalized muscle tremors, tetanic spasms and seizures.

Diagnosis

This relies on identifying hypocalcaemia and hyperphosphataemia in the face of low PTH levels. Biopsy of parathyroid tissue can confirm the diagnosis but is not usually necessary.

Treatment

Emergency treatment

Initial emergency treatment involves the immediate use of intravenous calcium gluconate (0.5–1.5 ml/kg of a 10% solution of calcium gluconate). This must be given slowly over 20–30 minutes with careful monitoring to identify any arrhythmias (either by electrocardiography or by pulse evaluation) and the infusion slowed or stopped if necessary. The use of subcutaneous calcium is not recommended

but there is also a significant risk of thrombophlebitis if intravenous calcium is given through a peripheral vein for extended periods or at high concentrations, or when there is extravasation from a catheterized vessel (Figure 16.12).

Chronic treatment

Lifelong replacement therapy is required in these cases. This is usually given in the form of vitamin D supplementation with or without oral calcium gluconate; the latter can usually be withdrawn once the animal has been stabilized.



16.12 The right hind limb of a Bichon Frise dog with primary hypoparathyroidism following treatment with intravenous calcium that extravasated from the intravenous catheter into the subcutaneous tissue. The limb was salvaged but it took many weeks of dressings and skin reconstruction.

Phaeochromocytoma

Phaeochromocytoma is an uncommon adrenal tumour in dogs and is even rarer in cats (Maher and McNiel, 1997). This type of endocrine tumour originates from chromaffin cells of the adrenal gland, the cells that synthesize catecholamines such as adrenaline (epinephrine) and noradrenaline (norepinephrine). The clinical signs of a phaeochromocytoma may be non-specific and may occur alongside other diseases in older animals, so the diagnosis of this condition is particularly challenging.

Clinical signs

These include episodic collapse, generalized weakness, weight loss, anorexia, intermittent panting, anxiety, depression and ataxia (Gilson *et al*., 1994; Bartez *et al*., 1997). The clinical signs usually reflect the pulsatile nature of the release of large amounts of catecholamines with their associated influence on blood pressure, cardiac output and heart rate. Animals may also have signs suggestive of systemic hypertension, including retinal haemorrhages, retinal detachment and epistaxis.

Cardiac abnormalities may include ventricular premature complexes, supraventricular tachycardia and atrioventricular block (Gilson *et al*., 1994).

Diagnosis

The ante-mortem diagnosis of phaeochromocytoma is difficult because of the variable nature of the clinical signs and the lack of a sensitive and specific test with which to confirm the diagnosis. There are no specific clinical pathology abnormalities but the finding of intermittent or sustained hypertension with an adrenal mass that is not secreting other hormone products (e.g. cortisol and its intermediates) is suggestive. However, phaeochromocytoma may coexist with adrenal or pituitary-based HAC, which could in itself explain the hypertension.

Measurement of plasma free metanephrines is the test of choice for the identification of phaeochromocytoma in humans and this test has recently been evaluated in dogs (Gostelow *et al*., 2013). Free metanephrine (fMN) and free normetanephrine (fNMN) concentrations were found to be predictive of phaeochromocytoma with good sensitivity and specificity (fMN had sensitivity of 62.5% and specificity of 97.3% when above the cut-off value, while fNMN had sensitivity of 100% and specificity of 97.6% when above the cut-off value). The availability of these tests should make the differentiation of phaeochromocytoma from other adrenal tumours easier in future.

Treatment

Management relies on reducing the systemic blood pressure and stabilizing the patient prior to surgical removal of the adrenal mass. Preoperative alpha-adrenergic blockade using phenoxybenzamine (0.2–1.5 mg/kg orally q12h) is useful as this drug is a non-competitive receptor antagonist. When there are significant cardiac arrhythmias, concurrent beta-adrenergic blockade is indicated, although this should never be introduced without prior phenoxybenzamine treatment otherwise severe hypertension results.

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Chapter 17

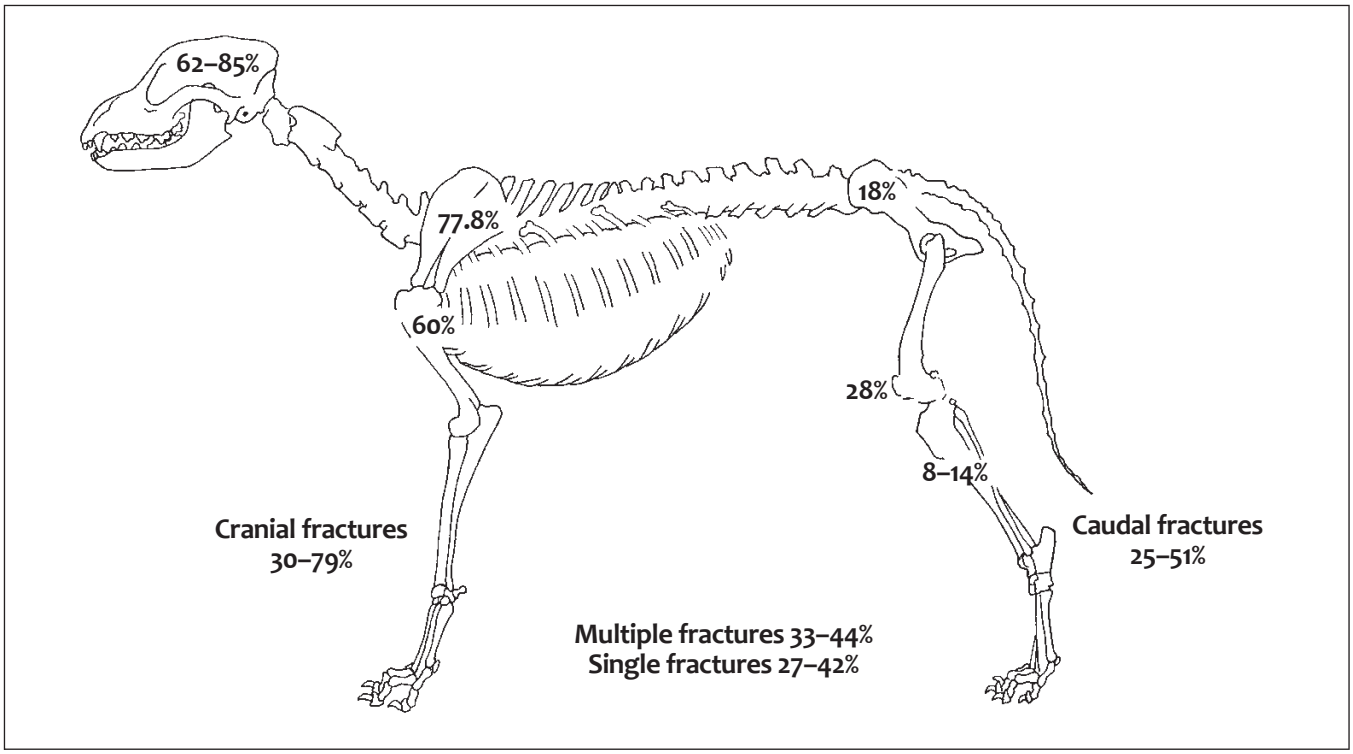
Acute management of orthopaedic and external soft tissue injuries

Sorrel Langley-Hobbs and Matthew Pead

Many animals with orthopaedic injuries or wounds also have injuries to vital organ systems. Fractures and wounds are often obvious and may be spectacular but must initially be assigned a low priority in emergency treatment, as they are rarely life-threatening. Concurrent injuries, especially those involving the thoracic and abdominal cavities, commonly occur during the trauma. The thoracic problems most frequently encountered include pulmonary contusions (46–66%), pneumothorax (12–50%) and rib fractures (10–25%) (Spackman *et al*., 1984; Tamas *et al*., 1985; Houlton and Dyce, 1992; Griffon *et al*., 1994; Sigrist *et al*., 2008) (Figure 17.1). If triage evaluation determines that there is any change in respiratory rate or effort, oxygen should be supplemented immediately.

If the animal is in shock, the cardiovascular instability should be addressed prior to any investigations or even a full physical examination. Shock can result from internal injury or from the wound or fracture alone. Fluid loss in burns, or osseofascial haemorrhage in fractures, can be sufficient to lead to irreversible shock and death. Following vascular access and initiation of shock therapy, if needed, the initial investigative plan for a trauma case following a complete physical examination should include: conscious thoracic and abdominal radiographs; a focused assessment with sonography for trauma (FAST) scan (Lisciandro, 2011); an electrocardiogram (ECG); and evaluation of blood packed cell volume (PCV) and total solids. If abnormalities are detected, further investigations may be appropriate.

While potentially life-threatening problems are a priority, temporary and emergency management of wounds and fractures should not be ignored. Initial treatment should be directed towards prevention of any additional injury or deterioration at the site of trauma, minimizing contamination and improving patient comfort. Emergency management of wounds and fractures should control any systemic implications for the traumatized tissues and prepare them for the start of definitive treatment.



17.1 Schematic diagram illustrating the incidence of thoracic injuries associated with fractures in specific areas.

BSAVA Manual of Canine and Feline Emergency and Critical Care, third edition. Edited by Lesley G. King† and Amanda Boag. ©BSAVA 2018

Wounds

Wounds are tissue injuries caused by chemical, thermal or physical trauma. In most cases the skin is damaged and there will be variable involvement of underlying tissues. Particular consideration should be given to the major structures adjacent to the site (Figure 17.2).

Wound types

Wounds related to physical trauma

These wounds result from the breakdown of tissue by physical force and are the most common type seen in veterinary practice. Punctures, lacerations, shearing or degloving of the skin and the impact of projectiles may all cause wounds (see Figure 17.2). They may be complicated by the presence of a foreign body. Recognition of the type of wound can give an early indication of the treatment required (Figures 17.3 and 17.4). In general, the physical breakdown of the skin layer allows damage and exposure of the deeper tissues. The immediate concern is to control haemorrhage and minimize contamination. All wounds should be covered immediately with a sterile dressing to prevent further contamination from the patient and the hospital environment, as nosocomial infection can be more serious and difficult to eliminate than infection resulting from the original injury.



17.2 A puncture wound in a 5-year-old Lurcher. (a) The dog became non-weight-bearing 4 hours after a walk. (b) The foot was swollen and hot and there was splaying of the toes. After clipping, a small sealed puncture wound was identified on the dorsal aspect of the paw. Surgery was performed: the puncture wound was opened and the tract debrided and flushed; no foreign body was found. A 5-day course of antibiotics was prescribed postoperatively and the dog's lameness fully resolved.

Burns

Burns cause cell death and the subsequent breakdown of tissue integrity. Although common in humans, they are relatively rare in veterinary practice. In thermal and electrical burns, the build-up of thermal energy cannot be dissipated before the cells are disrupted. In chemical and radiation burns, cellular integrity is directly disrupted by toxic substances or ionizing radiation. In all types of burns, destruction of tissue may continue after removal of the source of the injury.

There can be a life-threatening loss of fluid in burn injuries, and emergency treatment is based on removal of the source of the injury and assessment of the severity of the burn to determine the need for fluid therapy. Partial-thickness burns involve the epidermis and a variable degree of the dermis. Full-thickness burns involve all skin layers. Partial-thickness burns eventually progress to show distinct areas of viable and non-viable tissue, but this can take up to 10 days to happen naturally. Full-thickness burns progress to form a brown or black eschar, which may become hard to the touch.

In general, any deep partial- or full-thickness burn involving more than 15–20% of the animal's surface will lead to major systemic complications requiring emergency supportive therapy (Pavletic, 1993). Burns are vulnerable to infection, and the same care must be taken to prevent contamination as would be exercised for an open wound.

Treatment of wounds

Although it is advisable to progress to definitive treatment of wounds as soon as possible, other more serious complications of trauma may take priority. Treatment of wounds can be divided into emergency procedures (which can and should be done as soon as possible) and the initiation of definitive treatment. In many cases it is possible to combine these procedures without compromising the animal. It should not be forgotten that wounds themselves might pose a considerable systemic threat to the patient, especially in terms of fluid loss. All animals with wounds should be evaluated for analgesic therapy.

Owners should be made aware as soon as is practical of the implications of treatment in terms of the time involved and the potential cost of definitive treatment. Continued effective communication is important throughout the period of treatment as severe wounds can take a long time to heal and can be very costly to treat.

Emergency treatment

Emergency treatment of wounds often takes place at the time of initial presentation, while involvement of other body systems is being assessed and stabilization of urgent problems is occurring. Analgesia should be initiated as soon as possible. The animal should be muzzled or restrained as necessary to prevent self-trauma or contamination of the wound, and to ensure that veterinary staff can treat the animal effectively without being bitten.

Haemostasis: Bleeding should be addressed first. Direct pressure can be achieved using a wad of sterile gauze swabs or a bandage, and will be sufficient in most cases to stop minor bleeding. The addition of adrenaline (epinephrine) 1:1000 solution (1 ml adrenaline solution with 4–5 ml of sterile saline) to swabs may facilitate haemostasis. Use of adrenaline is contraindicated at extremities, where prolonged vasoconstriction may lead to ischaemia and necrosis, and in the presence of cardiac dysrhythmias. Wounds can also be packed with haemostatic agents such as calcium alginate fibre or chitosan linear polymer (Celox®). With more profuse arterial haemorrhage, it may be necessary to use 'pressure point' haemostasis. Pressure points are sites where major arteries run superficially, such as the brachial and femoral arteries in the axilla and femoral triangle, respectively; digital pressure is applied over the pressure point proximal to the area of haemorrhage. Head, nose and oral cavity arterial bleeding can be controlled by applying direct digital pressure to the deep area ventral and directly adjacent to the angle of the mandible where the common carotid arteries give rise to the maxillary artery tributaries. Superficial pressure will occlude the jugular, linguofacial or maxillary veins, which can increase venous bleeding, so it is important to apply pressure accurately.

Area	Examples of injuries	Considerations and comments
Head	Cranial fractures	Impacted cranial fractures may need removal or elevation of fragments. Risk of meningitis
	Brain damage	Continual monitoring of neurological status required to detect deterioration that may require surgical decompression. Medical management (see Chapter 9)
Neck	Tracheal rupture	Pneumomediastinum and subcutaneous emphysema
	Recurrent laryngeal nerve damage	Assess laryngeal function by observation under a light plane of anaesthesia
	Cervical spinal cord injury	Assess neurological function, evidence of fracture/dislocation of cervical vertebrae
	Carotid artery severance	Emergency haemostasis
	Oesophageal injuries	Perform oesophagoscopy to evaluate for tears or foreign bodies. Consider placement of gastrotomy tube to divert food while healing occurs
Thorax	Fractured ribs, pneumothorax, pulmonary contusions	Often treat conservatively. Large wounds must be covered to allow lung expansion. Air may need drainage if severe or a tension pneumothorax. Supplement oxygen. Flail chest – bandage and delay treatment
	Ruptured diaphragm	Usually delay repair until systematically stable, unless there is respiratory distress or the stomach is in the thorax
Appendicular	Bone, ligament, tendon, nerve, artery and vein	Check integrity of tendons, nerves (including spinal cord) and vasculature prior to anaesthesia and surgical intervention
Abdomen	Damage to any abdominal viscera. Abdominal wall or diaphragm rupture with herniation	Monitor for damage by regular physical examination, auscultation, ultrasonography and abdominocentesis. Biochemical and cytological analysis of blood and peritoneal fluid

17.3 Approach to management of wounds affecting specific areas.

Wound type	Description	Treatment considerations
Abrasion	Superficial wound involving destruction of varying depths of skin by friction or shearing forces. Usually bleeds minimally	When associated with a fracture, normal skin barrier is incompetent – treat fracture as grade I open
Avulsion	Characterized by tearing of tissues from attachments and creation of skin flaps. Limb avulsion injuries with extensive skin loss are called 'degloving'	Blood supply to skin may be compromised, leading to skin necrosis 2–5 days after injury. Repeat examinations and consider secondary debridement
Bite wound	A wound received from the teeth of an animal. Can cause a combination of puncture wounds, penetrating trauma, tears and crushing of tissue	Serious haemorrhage can occur if major vessels are pierced. Infection can occur from the pathogens in the biter's mouth
Burn – chemical	Direct exposure to noxious chemicals	Copious lavage to remove chemical. Ensure animal cannot lick area and ingest harmful substances
Burn – thermal	May see reddened, crusted or blackened skin. Burn injuries around the head and neck may compromise respiration	Beware of systemic complications of the burn. Attend to analgesia and cooling the area
Contusion	Blunt trauma may cause blood to pool in the subcutaneous tissue	Application of cold and analgesics. Beware of compartment syndrome
Crushing injuries	Combination of other injuries with extensive damage and contusion to the skin and deeper tissues	Assess neurological and vascular supply prior to treatment
Gunshots	These are contaminated. The heat generated in firing a bullet does not render it sterile. Open fractures may be present	Remove metal if encountered but not usually necessary to remove all fragments unless intra-articular or impinging on major structures such as nerves and arteries. Antibiosis for severe or intra-articular injuries. 'Treat the wound not the weapon'
Laceration	Created by tearing, which damages the skin and underlying tissues and may be superficial or deep and have irregular edges	Debridement and primary closure may be used if treatment is early
Penetrating foreign body	Foreign bodies such as sticks and glass can fragment, causing widespread contamination	May need extensive exploration to remove all fragments (90% of glass shards show on radiographs). Protruding foreign bodies should be left in place for transport but can be cut 2–3 cm from the body wall to minimize further internal damage by preventing the protruding shaft acting as a fulcrum
Penetrating trauma (e.g. stabbing)	Penetrating trauma is an injury that occurs when an object pierces the skin and enters a tissue of the body, creating an open wound. There may be an entry and exit hole	If abdominal or thoracic wound, check vital signs as there may be significant haemorrhage. Penetrating abdominal wounds require exploratory laparotomy
Puncture wound	A puncture wound is caused by an object piercing the skin and creating a small hole, which can be closed over and be barely visible. There is no exit wound. Damage can be superficial or deep	Infection may occur as the small puncture in the skin rapidly seals over. To treat the injury, the hole may need to be enlarged and opened, and the wound may need exploration for a foreign body such as a splinter

17.4 Recognition and treatment of specific wounds.

Pressure cuffs and tourniquets: Blood pressure cuffs may be placed proximal to appendicular wounds and inflated 20–30 mmHg higher than measured arterial pressure. These should not be left in place for more than 3–6 hours, or irreversible neurovascular compromise will occur. Tourniquets made from narrow bands of elastic material, such as Penrose drains, will place excessive pressure on neurovascular structures and may cause permanent deficits. They are not recommended unless the limb is to be amputated, or unless they can be applied distal to the tarsus or carpus where major motor nerves are not present. However, even in these sites, narrow tourniquet bands can still safely be used for only 3–5 minutes; in contrast, bands 5–10 cm wide can be used for up to 30 minutes. Ligation, surgical stapling and electrosurgery may then be used for definitive haemostasis. Profuse haemorrhage will require clamping and ligation of major vessels; lesser haemorrhage can usually be controlled by the application of a pressure bandage (Feliciano, 1992).

Initial control of contamination: A 'golden period' of 6 hours is said to exist, in which a contaminated wound may be cleaned and primarily closed or covered without development of infection. The procedure for cleaning wounds is summarized in Figure 17.5. Sterile apparel (especially gloves) and instruments should be used to minimize further contamination. A large volume of lavage fluid (minimum 500 ml) is used to remove contaminants, debris and bacteria, and to rehydrate the tissues. The pressure at which the fluid is applied should be sufficient to dislodge contaminants, but not excessive, as applying fluid under too high a pressure and inserting the needle deep into the wound will force contaminated or foreign material deeper, and open up uncontaminated tissue planes. Fluid applied through a 20–50 ml syringe with a 19 G needle will produce a satisfactory pressure of 48–62 kPa (7–9 psi), and will significantly decrease the number of bacteria and thus the incidence of infection. The ideal flushing solution should enhance bacterial removal without being toxic to the tissues. In one *in vitro* study neither phosphate-buffered saline nor lactated Ringer's solution caused any significant fibroblast damage compared with normal saline and sterile tap water. Lactated Ringer's may be the lavage solution of choice in the clinical situation (Buffa *et al*., 1997). Concentrated detergents and soaps are cytotoxic, as are some antiseptics; however, chlorhexidine (0.05%), povidone–iodine (0.01–1%) or polyhexanide/betaine (Wilkins and Unverdorben, 2013) are relatively non-toxic and safe to use. In wounds with gross contamination, tap water can be used, followed by a sterile lavage solution. However, topical agents such as wound powders, intramammary preparations, hydrogen peroxide and alcohol should be avoided. These substances cause cell death, provoke a foreign body reaction and interfere with the healing process. Finally, the wound is again covered with a sterile dressing. Time spent minimizing contamination (and thus preventing the establishment of infection at the earliest possible stage) can significantly shorten the healing time of wounds.

- Haemostasis
- Cover wound with sterile dressing whilst preparing for lavage
- Wear sterile gloves (and hat, mask, gown)
- Apply gel or sterile saline-soaked swabs to the wound
- Clip away hair, working from wound outwards if possible
- Flush wound with sterile saline, remove all contaminants from chemical burns
- Take a bacterial swab for culture
- Apply a sterile dressing and bandage

17.5 Summary of emergency wound care.

Emergency treatment of burns: Evaluation of the area of a burn is critical; thorough and wide clipping of the area is essential. The damage related to a burn and the surface appearance may change in the first 48–72 hours, therefore the clipped area should be regularly reassessed. Burns may initially appear as reddened areas of inflamed skin with a crust or scab over the surface. The hair may fall out or be easily plucked from full-thickness burns. Partial-thickness burns may be painful when touched; conversely, full-thickness burns are typically non-painful as peripheral nerve endings are destroyed. Once the area has been assessed, aggressive fluid therapy should be started if the burnt area exceeds 15% of the body surface. In humans the burn surface area is estimated by the 'rule of 9s', but adapting this rule to dogs is not accurate, because when considering the elastic redundant skin covering many dogs, there is a tendency to overestimate the surface area involved (Pavletic and Trout, 2006). Patients should be assessed for evidence of dehydration, anaemia and hypoalbuminaemia. Monitoring the bodyweight, heart rate, arterial and central venous pressure and urine output assists in regulating fluid therapy. Cardiovascular, pulmonary and renal function should be evaluated and monitored for several days following the injury.

The area of the burn can be cooled by lavage, and in chemical burns all residues should be washed away with copious volumes of water. Large burns should be cooled with care in order to prevent severe heat loss in a debilitated patient. Application of soaked dressings or gentle flushing with fluid at 3–10°C for at least 30 minutes is recommended. The necrotic skin in the eschar has great potential for infection and will not be penetrated by systemic antibiotics. Until this tissue can be removed, it should be protected with topical antibiotics, particularly silver sulfadiazine in a water-soluble cream, and covered with a sterile non-adherent dressing. Definitive treatment is initiated using principles and techniques common to the management of other wounds. These are described later in the chapter.

Emergency treatment of gunshot wounds: Gunshot wounds to the limbs not associated with a fracture can be treated conservatively. Animals with evidence of peritoneal penetration require an exploratory laparotomy to determine the degree and level of organ damage and to repair defects. Animals with thoracic injuries can usually be managed with conservative treatment or thoracocentesis, but if pneumothorax or haemothorax does not resolve with conservative treatment a thoracotomy to assess and address damage may be required. Wound infection can develop after gunshot, and initial treatment of animals with gunshot wounds should include obtaining cultures followed by administration of antibiotics effective against Gram-positive and -negative bacteria (Fullington and Otto, 1997).

Starting definitive wound treatment

Once the animal is stable and other injuries have been addressed, definitive treatment can be initiated (Figures 17.6 and 17.7). Thorough treatment normally requires analgesia and general anaesthesia. The nature and extent of the wound should be evaluated and a plan for subsequent preparation and treatment devised. Such a plan will depend on the nature of the wound (see Figure 17.4). Wounds should be treated in an aseptic fashion using sterile technique and sterile apparel. A large



17.6 Early management of a dog with bilateral fractures, prior to surgical stabilization. (a) Craniocaudal and (b) mediolateral views of a grade I open radius and ulna fracture; air is visible under the skin shadow adjacent to the fracture on the medial aspect. (c) There is a closed distal humeral supracondylar fracture in the left forelimb. (d) Small wound associated with the open fracture prior to treatment. (e) Using aseptic technique whenever possible, water-soluble jelly is applied to the wound prior to clipping to prevent hair entering the wound. (f) The wound is flushed with a 19 G needle, 20 ml syringe and lactated Ringer's solution. (g) A splinted bandage is applied to support the grade I open radius and ulna fracture. (h) A spica splint is applied to support the supracondylar humeral fracture. (i) Definitive stabilization of the radius and ulna fracture is achieved with a type 1b external skeletal fixator once the patient is stable for anaesthesia. A non-adherent dressing (e.g. Primapore) is applied to the small wound.

- Aseptic technique
- Evaluation and treatment plan
- Preparation of skin and surrounding area
- Debridement
- Lavage
- Bacterial culture and evaluation of contamination
- Evaluation and execution of closure if appropriate
- Administration of appropriate antibiotics
- Application of a sterile dressing and bandage

17.7 Summary of initial definitive wound care.

area of normal skin around the wound should be clipped to allow a thorough inspection and to prepare for definitive surgical treatments, such as the use of skin flaps (Mayhew, 2009). The skin is scrubbed thoroughly using a proprietary scrub solution. Any exposed areas of the wound can be protected during this initial phase by covering them with a water-soluble gel or swabs soaked in sterile saline. Water-soluble gel can be lavaged away together with any debris from the clipping and preparation.

Debridement:

1. Remove all foreign debris such as gravel and superficial gunshot (tissue should not be aggressively explored to retrieve all shot).
2. Dissect out and remove obviously necrotic tissue, especially muscle, fat and skin. Nerves, blood vessels, tendons, ligaments and bone with soft tissue attachments should be preserved.
3. Leave tissue that has a good chance of viability, especially when major structures are involved or the wound involves the distal extremities. If viability is questionable, a delayed debridement can be performed several days later if necessary.
4. Remove partial-thickness burn eschar by 'tangential section', sharply cutting back the tissue parallel to the surface until healthy bleeding dermis is encountered.
5. Debride full-thickness burn eschar vigorously, as early as possible, to define its extent.
6. Control haemorrhage carefully, as blood provides the ideal conditions for bacterial proliferation. Use pressure and diathermy where possible, with ligation for larger vessels.
7. Lavage the wound with sterile saline as described above.
8. Take a swab for culture at the end of cleaning and debridement, as this timing has been found to produce the most significant results.

Decisions on the amount of tissue to remove can be difficult. The most common cause for delayed wound healing and infection is inadequate debridement, therefore aggressive debridement, especially with expendable structures, is often the best policy. There is some variation in recommendations for different types of tissue, and the following general guidelines are useful:

- Assess skin viability based on colour, temperature, bleeding, palpation for distal pulses on extremities and pain sensation. Non-viable skin will appear black, blue-black or white, feel cool, lack pain sensation and will not bleed. Skin of questionable viability may appear blue or purple
- Debride muscle until it bleeds and contracts following appropriate stimuli
- Remove small bone fragments from open fractures, as they may prevent complete granulation
- Excise contaminated fat aggressively as it is easily devascularized, harbours bacteria and is expendable.

Other techniques that have been used to assess tissue viability include dye injection, the use of radiographic contrast media, transcutaneous oxygen and carbon dioxide measurements, and laser and colour flow ultrasonography or Doppler velocimetry (Bellah and Krahwinkel, 1985; Rochat *et al*., 1993). However, visual examination is feasible in most situations and was found to be as accurate as dye infusion in one study (Bellah and Krahwinkel, 1985).

Assessment of bacterial contamination: When to close a wound and whether to prescribe antibiotics is influenced by the degree of bacterial contamination. Swabbing for culture and sensitivity at the end of debridement and lavage is sufficient for most wounds healing by second intention, as antibiotic therapy can be targeted accurately. However, infection is a significant source of morbidity in prematurely closed wounds, and further precautions may be needed if closure is contemplated. Gross inspection will not determine whether a wound is infected or not, but quantitative bacterial counts and culture can provide insights into the advisability of wound closure. If there are $>10^5$ organisms/g or beta–haemolytic streptococci present, then the wound should not be closed (Gfeller and Crowe, 1994). The rapid slide test (RST) can be performed prior to attempting wound closure. The method involves swabbing 1 cm^2 of the deepest surface of the prepared wound with a sterile cotton-tipped swab. The swab is rubbed over 1 cm^2 of a clean microscope slide. The slide is examined under microscopy and if even one bacterium is seen, the wound should not be closed (Gfeller and Crowe, 1994).

Closure: After cleaning and debridement and assessment for infection, the wound may either be closed immediately (primary), left for 3–5 days and then closed (delayed primary), closed after the granulating bed has matured in approximately 10 days (secondary closure), or left to heal by granulation and re-epithelialization (second-intention healing). The wound should only be closed if there is confidence that all necrotic tissue and debris have been removed and if closure can be achieved without excessive tension. Tension-relieving techniques, such as undermining, walking sutures, subdermal suture patterns (inverted vertical mattress pattern), vertical mattress sutures, far–near–near–far and far–far–near–near suture patterns, stented sutures, relaxing incisions, bipedicle flaps, V–Y plasties or Z plasties, may be useful in closing selected wounds (Williams, 2009).

For wound repair, a small-diameter monofilament non-absorbable suture material should be selected, although, if available, stapling is faster than suturing. Wounds treated by primary closure should initially be covered, as it takes 24–48 hours for a fibrin seal to form that will resist bacterial invasion. Unpublished studies suggest a 50% higher infection rate in uncovered wounds. For selected wounds, drainage should be provided because wound fluids and exudates interfere with normal healing. A drain can be used for dead space obliteration, to eliminate established fluid, and for prophylactic prevention of fluid or air accumulation within a wound. Active suction drains are particularly useful under these circumstances (Bellah and Krahwinkel, 1985; Rochat *et al*., 1993). In-depth discussions of protracted wound management and surgical reconstruction of wounds can be found in the *BSAVA Manual of Canine and Feline Wound Management and Reconstruction* as well as other specialized texts (e.g. Pavletic, 2010).

Selection of antibiotics: Clean wounds primarily closed within 6–8 hours of the injury, and more extensive wounds correctly treated with debridement and lavage, do not need antibiotic therapy provided tissue damage is minimal. Antibiotic therapy is indicated in the management of wounds where treatment is delayed more than 6–8 hours, deep wounds involving muscle, wounds with severe tissue damage or where tissue of doubtful viability is left after debridement, and in patients with systemic infection or immunocompromise. If antibiotics are given in the first 3 hours after injury, they will contact bacteria via the fluid in the wound, before debris and fibrin surround them. To exploit this opportunity, intravenous therapy should be started as soon as possible to maximize antibiotic levels in tissue and wound fluid. As results from culture will not be available at this stage, simple guidelines are used to select a broad-spectrum antibiotic. Most wounds are exposed to contamination from

Staphylococcus and *Streptococcus* species. Bite wounds may contain *Pasteurella* and Gram-negative species such as *Escherichia coli*. Gram-negative species may also be found in puncture wounds and in potentially contaminated areas such as the perineum. Cephalosporins, trimethoprim/sulphonamides, co-amoxiclav and enrofloxacin all have activity against these organisms and can be given intravenously. When there is a possibility of extensive Gram-negative contamination, an aminoglycoside should be considered. The results of the RST can also be useful in appropriate antibiotic selection. In one study on bacterial resistance in *Staphylococcus* spp., the highest frequency of resistance was observed for penicillin, followed by ampicillin, tetracycline and chloramphenicol. The highest frequency of resistance in *E. coli* isolates was recorded for tetracycline and streptomycin. *Pasteurella* spp. and *Streptococcus canis* had the highest resistance rate for tetracycline and chloramphenicol (Awji *et al*., 2012).

During definitive treatment, antibiotic therapy can be modified on the basis of culture results. Unless there is an indication to change or extend the course, the most effective, narrowest-spectrum, cheapest and safest antibiotic available should be continued by injection or orally for 5–7 days. If the appearance of the wound does not improve or the patient's systemic condition deteriorates, a change in antibiotics coupled with re-swabbing the wound for repeat culture and sensitivity testing is indicated. Antimicrobial medication can usually be discontinued once a good granulation bed has become established (Figure 17.8).

Systemic antibiotics alone will be adequate in most situations, but heavily contaminated wounds and burns are best treated with a combination of topical and systemic therapy (Figure 17.9). Gentamicin, nitrofurazone, bacitracin/polymixin and neomycin may all be delivered to the wound via the primary dressing layer. Topical antibiotics or antiseptics are particularly useful when the contaminants are resistant or difficult to treat systemically, such as



17.8 (a) Avulsion or shear injuries on the medial aspect of a dog's antebrachium and carpus. (b) The same dog 10 days later. After the use of wet to dry dressings, and then non-adherent dressings, healthy granulating tissue is present with evidence of early epithelization and wound contraction. At this stage antimicrobial therapy should no longer be necessary.

- For simple wounds, which are treated correctly, do not use antibiotics
- For serious wounds, start broad-spectrum intravenous therapy immediately
- Reassess therapy on the basis of culture, rapid slide test results, wound progress and the patient's condition
- Once therapy is started, continue for 5–7 days
- Consider combinations of multiple systemic and topical drugs in heavily contaminated wounds with resistant bacterial species

17.9 Summary of antibiotic selection.

Pseudomonas spp. Soaking the primary dressing in tris-EDTA (ethylenediaminetetraacetic acid – tromethamine) also aids the control of *Pseudomonas* (Farca *et al*., 1997). Tris-EDTA is made by combining 1.2 g of EDTA with 6.05 g tris (a buffer), added to 1 litre of sterile water for injection. The pH is adjusted to 8.0 using dilute NaOH solution and the resulting tris-EDTA solution is autoclaved for 15 minutes. Topical water-soluble silver sulfadiazine cream can be applied to the eschar in burn cases, to prevent the necrotic tissue becoming infected.

Dressings and bandages

Dressings are required as a primary contact layer with the wound. Maintaining the apposition of the wound, provision for the storage of exudates and mechanical stability can be achieved using various combinations of bandages, adhesives, sutures and external skeletal fixation (ESF). Individual bandages and slings are addressed in the section on musculoskeletal trauma. The principal decision relates to the choice of dressing; selection of appropriate dressings depends on evaluation of the state of the exposed tissue, the degree of contamination and the anticipated production of fluid from the wound surface (Figure 17.10). Ideally, a dressing should:

- Prevent further contamination
- Assist the process of debridement
- Conduct fluid away from the surface, preventing pooling, maceration and the formation of an environment conducive to bacterial proliferation
- Prevent desiccation and maintain a moist, well oxygenated environment to promote repair.

The primary consideration for initial management of wounds is whether to use an adherent or non-adherent dressing. Adherent dressings, such as dry swabs or sterile saline-soaked swabs that are allowed to dry in contact with the wound (wet to dry), aid debridement (Figure 17.11). Such dressings are useful in wounds that have a considerable amount of necrotic debris and where surgical debridement is delayed. However, they can be painful to remove and removal may disrupt granulation tissue. The wound surface may become desiccated if the dressing is too dry, and macerated if it is too wet. Non-adherent dressings prevent disruption and damage to epithelializing or granulating tissue at removal. They vary in their degree of absorbency, and conduct fluid away from the surface to a greater or lesser extent (see Figure 17.15a). In addition, some of them have interactive properties that promote the removal of necrotic debris and bacteria from the wound surface, but they are not as valuable in the process of debridement as the adherent dressings. Non-adherent dressings are easier to manage, less painful to change and maintain a more constant wound environment.

Description (and proprietary examples)	Properties	Uses	Contraindications
Thin perforated polyester film, backed with absorbent cotton and acrylic fibre pad (Melonin, Smith & Nephew; Primapore, Smith & Nephew; see Figure 17.6i)	Semi-occlusive Non-adherent May have adherent surround, e.g. Primapore	Clean sutured wounds, abrasions, lacerations and minor burns	Necrotic wounds or those requiring debridement
Open-weave gauze impregnated with paraffin jelly (Jelonet, Smith & Nephew)	Non-adherent Free draining into absorbent secondary dressing May be antibiotic impregnated	Low-viscosity exudative wounds	Avoid on granulating wounds as interdigitates with expanding granulating tissue, which causes damage at removal
Outer polyurethane film, hydrophilic core, polyurethane wound contact layer (Allevyn, Smith & Nephew; see Figure 17.15a)	Non-adherent Controlled exudate absorption Absorbs 10 times its own weight Keeps wound moist	Granulating wounds with some exudation Can be left in position for up to 5 days	Necrotic debris
Hydrocolloid gel (Intrasite, Smith & Nephew; Granuflex, ConvaTec Ltd)	Moist environment Non-adherent Interactive, conformable Waterproof (Granuflex) Absorbs exudate	Granulating wounds, including those with some necrotic debris Can assist in microdebridement Vehicle for antimicrobial agents, e.g. metronidazole	Highly exudative wounds
Calcium alginate fibre (Kaltostat, ConvaTec Ltd)	Interactive ion exchange Haemostatic Absorbs 20 times its own weight	Bleeding and exudative wounds	Dry wounds or wounds with necrotic slough
Open-weave gauze saturated with sterile saline Wet to dry or wet to wet (see Figure 17.11b)	Adherent Saline dilutes exudate and facilitates absorption Debriding – necrotic material entrapped as gauze dries, and removed at dressing change	Open degloving wounds, especially if contaminated or necrotic. Use in early stages to aid debridement, soak with tris-EDTA and antibiotics or perfuse solutions to moisten dressing continuously	Healthy granulating epithelializing wounds

17.10 Characteristics of a variety of dressing materials.



17.11 (a) This wound over a dog's carpus occurred as a result of a dogfight. There is some granulation tissue present but further superficial debridement of the necrotic mucoid layer would be beneficial. (b) 'Wet to dry' dressings with sterile swabs soaked in sterile lactated Ringer's solution are applied to the wounds. (c) The appearance of the wound 24 hours after application of a wet to dry dressing. There has been superficial debridement of the wound and the granulation tissue now has a more healthy appearance.

Ideally, initial treatment of most wounds should be with an adherent dressing to assist micro debridement, followed by non-adherent dressings once granulation commences. However, to ease the management of dressing changes, in many cases non-adherent dressings can be used throughout the healing process. Recent improvements in the properties and variety of these dressings, particularly the ability of some of them to participate in microdebridement, allow selection of a dressing with properties appropriate to the stage of wound healing. Whatever dressing materials are used, a schedule for dressing changes should be devised based on the severity of the wound. Frequent dressing changes allow more accurate monitoring, but may retard healing and distress the patient. In addition, sedation may be required for dressing changes, which will necessitate repeatedly withholding food from the patient and therefore may interfere with its nutritional needs. Dressings on contaminated wounds and those with severe skin loss should be changed within the first 24 hours. Dressings over simple lacerations should be changed after 48–72 hours. Removal of adherent dressings can be painful; pain can be ameliorated by soaking the primary layer with sterile saline or 2% lidocaine. The protocol described for initial wound management, particularly the need to maintain asepsis, should be followed as far as possible at dressing changes.

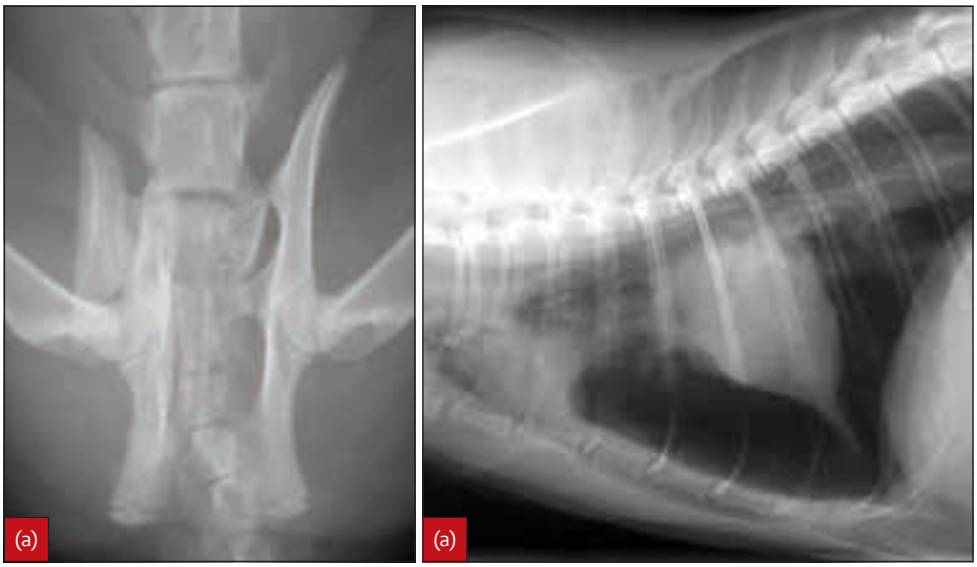
Vacuum-assisted closure

Vacuum-assisted closure (VAC) or negative pressure wound therapy (NPWT) has been widely used in human medicine and is now being used in veterinary patients for acute, chronic and infected wounds. The technique involves the application of sub-atmospheric pressure to a wound via the application of an open-pore foam dressing. The technique has been shown to accelerate granulation tissue formation, increase wound contraction and assist with infection control (Owen *et al.*, 2009). NPWT can be applied immediately after emergency management and stabilization of the patient. In one report of dogs being admitted with

distal limb injuries, NPWT was applied once emergency treatment of the patient had been instigated; the perceived benefits were that the dogs required fewer dressing changes, there was a shorter time between wounding and definitive treatment such as skin graft, and therefore an overall shorter hospitalization time (Ben-Amotz *et al*., 2007). In an experimental study NPWT accelerated the appearance of smooth, non-exuberant granulation tissue; however, prolonged use of NPWT impaired wound contraction and epithelialization, so there appears to be no benefit in continuing NPWT after a smooth granulation tissue bed has become established, which occurs within approximately 10 days in most cases (Demaria *et al*., 2011).

Musculoskeletal trauma

Although they are often the most obvious and impressive part of a case, musculoskeletal injuries have a low priority in the initial handling of the trauma patient, and emergency care must be directed primarily towards systemic injuries. Even after evaluation of the major organ systems, musculoskeletal injuries cannot be considered in isolation. The haemorrhage and local disruption of the surrounding soft tissue may pose more problems than the injury itself, therefore the integrity of all tissue involved and its systemic implications must be considered before definitive fixation (Figures 17.12 and 17.13).



17.12 Prioritization of therapy: radiographs of a cat which had recently been involved in a road traffic accident. (a) The cat had a displaced ilial fracture and a sacroiliac luxation; it was unable to ambulate and had neurological deficits. (b) However, the cat was also in respiratory distress with a tension pneumothorax, which required emergency thoracocentesis.



17.13 (a) A 3-year old female cat was referred with an open tarsal dislocation and fracture after a suspected road traffic accident. (b) The cat had a palpably enlarged abdomen with a fluid thrill on percussion. An ultrasound scan revealed free abdominal fluid and a small bladder. (c) A positive contrast cystogram showed leakage of contrast medium into the abdomen, changes compatible with a tear in the bladder.

Definitive treatment frequently requires a prolonged period of anaesthesia to allow accurate evaluation and corrective surgery. Most definitive treatment should thus be outside the remit of emergency care and the reader is referred to other texts such as the *BSAVA Manual of Canine and Feline Fracture Repair and Management*. However, the emergency management of a specific injury can be important in improving the systemic condition of the animal and managing pain, and therefore can have as much impact in achieving complication-free healing as definitive fixation.

Fractures and luxations

Most fracture or luxation presentations are simple, acute and have a clear history or there is a high index of suspicion (e.g. the animal has been missing) of external trauma. Clinical signs include pain, deformity, swelling, crepitus and instability. The systemic consequences can be severe. The osseofascial haemorrhage that occurs in closed femoral and humeral fractures can result in up to 30% of circulating blood being sequestered at the fracture site. Fractures and luxations that occur without extensive direct trauma require less consideration of systemic problems in the early phase of treatment. These include isolated luxations (both traumatic and congenital or developmental) and simple fractures, such as condylar fractures in puppies that occur when a shear force is transferred indirectly to the bone by an axial compression force along the antebrachium. In these cases, investigation can progress more rapidly to a definitive evaluation of the fracture or luxation and the underlying cause, once simple support and analgesia have been implemented.

Evaluation

There are numerous systems for the evaluation and classification of fractures. These systems are mostly used in decisions related to definitive treatment, rely on accurate imaging and are unnecessary for initial treatment. A basic evaluation should therefore be made of the position of the injury, its relationship to critical structures and whether it is open or closed. The accompanying systematic examination should include a general evaluation of the extremities, assessing pulses, neurological status and the presence of wounds or devitalized skin. Oedema indicates impaired venous and/or lymphatic return caused by acute inflammation, haematoma or mechanical impingement. On the basis of this information, the problem can be categorized in the following manner:

- Fractures and luxations that require prompt treatment due to life-threatening complications (impacted cranial fractures, spinal fractures/luxations and open fractures involving major structures)
- Fractures that will benefit from being treated immediately, provided the animal is not at increased risk from anaesthesia (open fractures and luxations)
- Fractures that should be treated within 24–48 hours for optimal results (articular and epiphyseal fractures and all other luxations)
- Fractures that need to be treated within 5 days of occurrence (all other fractures).

Evaluation of position: Although evaluation of abnormal range of movement, swelling and crepitus is useful, manipulation and palpation of fractures or luxations should be minimized to prevent discomfort and further damage to adjacent tissue. If the animal will lie quietly, it is often possible to take a survey radiograph to give information on the position and extent of the injury. Even though such radiographs may not be accurate enough for use in the definitive fixation, they are often the best and least distressing method of evaluating the position of the fracture.

Evaluation of open fractures: The main feature of open fractures is that there is direct exposure of the bone to the outside environment. Evaluation of the grade of open fracture, allows straightforward selection of therapy and an early indication of prognosis. The guidelines for evaluation are:

- Grade I: Penetration of the skin by a bony fragment from the fracture. The fragment frequently retracts back beneath the skin. Prognosis is as good as for a closed fracture, providing that there is aseptic wound handling and early fixation
- Grade II: The fracture is created by an external force, which also creates a wound. The bone is not directly exposed but communicates with the wound and there is variable damage and/or loss of skin and underlying tissue. Prognosis depends on the degree of soft tissue loss and contamination
- Grade III: Severe injuries that are commonly associated with high-energy trauma. The fractures are often comminuted and there is a high degree of tissue loss, contamination and devitalization. Bony union is normally delayed and there are often complications during the healing period.

The prognosis in grade III fractures is variable. In some cases it may not be possible to treat the fracture successfully and initial treatment should be aimed towards an amputation. In humans, the grade III group has been further subdivided to help in this decision (Caudle and Stern, 1987):

- Grade IIIA: Despite extensive soft tissue loss and/or high-energy trauma, there is still adequate soft tissue covering bone. There is a fair prognosis despite extended healing time
- Grade IIIB: Soft tissue loss is more severe with exposure of bone and periosteal stripping present; often highly contaminated. The prognosis is guarded and in some cases will force amputation
- Grade IIIC: There is severe tissue damage with major arterial damage. The prognosis is poor and amputation should be considered.

Distal limb injuries: Distal limb injuries are relatively common in dogs and cats. The major problem with these injuries is often the shear or degloving wound, which may be large and extend around much of the circumference of the limb. Fractures and luxations may also be present. Emergency treatment involves management of the large open wound (which is often contaminated) and support of the associated orthopaedic injuries. The viability of the limb must be assessed, as in severe cases there may be such disruption and damage that the vascular supply to the distal limb is inadequate to maintain viability to the appendage. Visual assessment of the colour of non-pigmented pads and needle pinpricks can be used to assess bleeding. However, the clinician should be aware that extremities will appear cold and pale in animals with shock or hypothermia, and clinical examination should be repeated regularly as resuscitation proceeds. Needle pinpricks should also be interpreted with caution in these

circumstances; bleeding due to venous stasis or coagulopathy may be misleading. Needle pinpricks can also introduce infection into healthy tissue (Anderson and Langley-Hobbs, 2013). Angiography is the definitive way to determine the viability of arterial supply to the distal limb. However animals with this level of injury may not be suitable candidates for long procedures under anaesthesia and intravenous contrast agents are contraindicated when the systemic circulation is compromised in any way (Anderson and Langley-Hobbs, 2013). A limb with loss of arterial supply will need amputation; this will most commonly be a total amputation of the whole limb. However, if the owners would like the animal to be fitted with a prosthetic limb or an intraosseous transcutaneous amputation prosthesis (ITAP), a partial amputation should be performed. The advice of a surgical specialist should be sought at an early stage in this scenario.

Principles of emergency treatment of fractures and luxations

The principles of emergency management of fractures and luxations consist of:

- Provision of analgesia
- Increasing patient comfort and minimizing movement (Figure 17.14)
- Prevention of further compromise of blood supply
- Limiting further soft tissue damage resulting from instability
- Limiting swelling
- Treating wounds over open fractures in the same way as described previously for other wounds.

Application of these principles is primarily dependent on the position of the injury. Some techniques for fracture management are valid for one area and wholly inappropriate for another.

Bone affected	Method of stabilization
Mandible	None, or tape muzzle
Maxilla and cranium	None
Cervical spine	Neck splint
Scapula or humerus	None or full spica splint (see Figures 17.21c and 17.22a)
Radius and ulna or tibia	Support bandage or splinted bandage
Carpus or tarsus and all bones distal	Support bandage
Thoracolumbar spine	Back splint (see Figure 17.24)
Caudal lumbar spine	None
Pelvis	None
Femur	None or a full spica splint

17.14 Emergency stabilization of fractures.

Open injuries should be considered as wounds involving a fracture or luxation. The same considerations of emergency treatment, debridement, contamination, antibiotics and dressings should be applied as outlined earlier. The depth of tissue involved in grade II and III injuries dictates the application of maximal care to these injuries. Early stabilization, where possible, reduces discomfort and can speed recovery. Temporary stabilization should always be considered concurrent with early treatment of the wound, as stability promotes wound-healing processes, decreases pain and reduces complications. External coaptation can be used if it is appropriate to the site. ESF is often the optimal definitive fixation for open fractures. However, ESF should also be considered during initial management, as an alternative to external coaptation. With appropriate training and experience, ESF can be placed fairly rapidly in a closed fashion. However, it is not something that is done routinely in emergency practice, and the time to consider application of ESF by a surgeon would be following initial wound management and stabilization of the patient, perhaps during anaesthesia for wound debridement. Unlike external coaptation, ESF allows the stability of the site to be maintained during dressing changes, thus reducing pain, the need for sedation for dressing changes and the amount of bandaging material required. Transarticular ESF (Figure 17.15) can be used to control the stability of a wound over a joint even when no fracture is present, for example, after a traumatic luxation with shear injury.



17.15 (a) The hock of the dog shown in Figure 17.8 with a dislocation and an avulsion or shear wound on the cranial flexor aspect of the hock. A non-adherent absorbent dressing (Allevyn, Smith & Nephew) and hydrocolloid gel (Intrasite gel, Smith & Nephew) have been used. (b) The same dog 10 days later, after stabilization of the hock with a transarticular external skeletal fixator and appropriate wound management consisting of daily wound flushing and application of 'wet to dry' or non-adherent dressings as dictated by the appearance of the wound.

Selection and use of bandages

Bandages can be used to stabilize traumatized areas and to hold dressings in place. However, it can be difficult to place bandages correctly on a distressed patient and the benefit of a bandage, particularly complex ones such as slings and spica splints (see Figures 17.16 and 17.21), must be weighed against the problems of possible incorrect placement. Simple bandages also have limitations. The Robert Jones bandage, when applied above the elbow or stifle, tends to slip down and form a 'pendulum' of extra weight at or below the joint. Thus, when considering emergency stabilization there are several situations in which it is better not to apply an extensive bandage, but to use cage rest, analgesia and sedation to restrict further damage at the fracture site (see Figure 17.14).

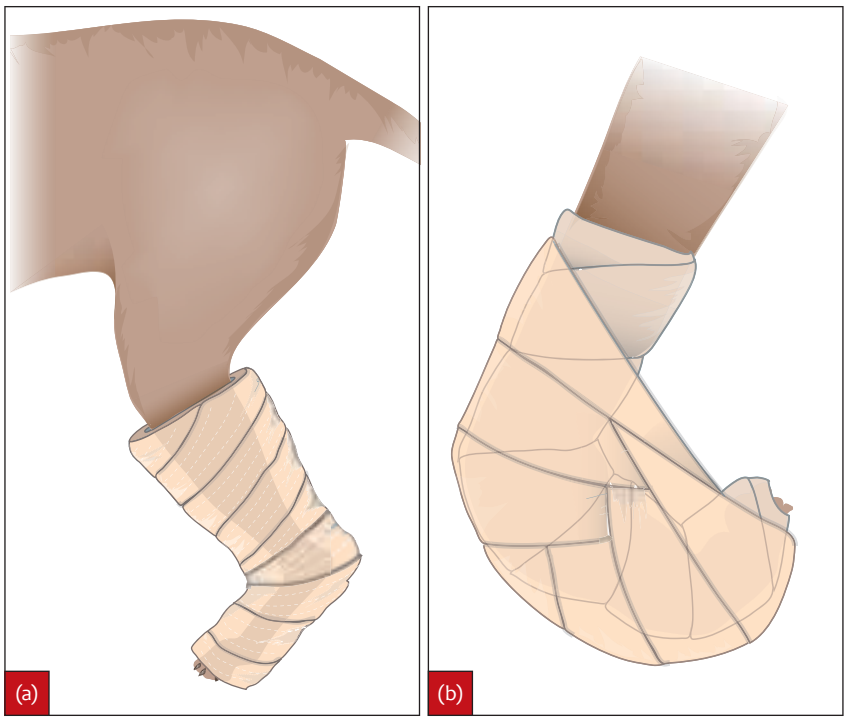
Specific situations in which certain bandage configurations are appropriate are outlined in Figures 17.16 and 17.19 and in the text below. Dressings can be held in place over

Type of bandage	Description	Uses	Comments and specific contraindications
Support (modified Robert Jones dressing)	Use deformable secondary layer applied under compression. Leave pads of middle two digits protruding to allow checking for swelling	Stable fractures distal to the elbow or stifle. Positioning of a dressing, especially over an exudative wound	Do not use in proximal limb fractures; rarely of use in elbow or stifle injuries. In these cases the bandage may slip down and become a pendulum weight
Splinted bandage	Augment a support bandage with a splint to increase rigidity without extra bulk	Unstable fractures distal to the elbow or stifle	Do not use in proximal limb fractures; rarely of use in elbow or stifle injuries
Velpeau sling	Bandage placed around leg and over body to flex carpus, elbow and shoulder	Holds entire forelimb in flexion to prevent weight-bearing and movement of distal limb	Provide sufficient padding to prevent sores
Carpal flexion	Figure-of-eight bandage applied over padding from distal radius to metacarpals	Flexion of carpus and prevention of forelimb weight-bearing, although limb can still be moved	Do not use for antebrachial or distal injuries
Ehmer sling	Figure-of-eight bandage from metatarsals to distal femur with the bandage all medial to the tibia	Internal rotation of hip and stifle reduces the chance of re-luxation after reduction of craniodorsal hip luxations	Difficult to apply, especially on cats or short-legged dogs
Hobble	Bandage connection between both distal tibias	Prevents abduction and reduces the chance of re-luxation after reduction of ventral hip luxations	
Spica splint	Flat splint strapped from toe to dorsum. Held in place with support bandage distally and body bandage	Fractures proximal to the elbow (use in hindlimb is also reported)	Not usually recommended for injuries distal to the elbow or stifle

17.16 Bandages (see also Figures 17.17, 17.18, 17.21 and 17.22).

the body with wraps, particularly using the newer elasticated and conformable materials. The most useful general configuration is the support bandage.

Support bandage: Support bandages minimize swelling and oedema, aid haemostasis, provide stabilization and increase patient comfort. True pressure bandages are rarely necessary and should never be left on for more than an hour. The Robert Jones bandage is known as a pressure bandage but, with the deformable materials used, pressure is generally not maintained for a significant length of time; the smaller, less cumbersome bandage is often referred to as a modified Robert Jones. Pressure gauges placed on the skin under such bandages soon return to normal. Support bandages should be applied with a primary layer covering any wound, a secondary layer of a conformable material such as cotton wool, a tertiary layer using a tightly wound bandage and an outer protective bandage. The bandage should be placed to follow the normal aspect of the limb (Figure 17.17) and can be reinforced by a splint placed after the secondary layer has been pressurized. Splints can be made from strips of cast material and therefore conformed and customized to the patient, but commercial off-the-shelf products are partiularly useful for temporary and emergency usage (Figure 17.18).



17.17 Bandaging the lower limb. (a) The Robert Jones bandage provides a column of support following the conformation of the limb. (b) The carpal flexion bandage prevents weight-bearing but allows movement of the upper limb joints (elbow and shoulder).



17.18 A commercial splint with Velcro tapes can be applied rapidly to provide temporary support during healing or while awaiting definitive repair.

Ischaemic injury

Ischaemic injury can occur after incorrect application of a bandage (Anderson and White, 2000). This is attributed to direct pressure necrosis related to inadequate or uneven application of padding, or to a tourniquet effect resulting in secondary ischaemic oedema. All owners of cases discharged with bandages in place should be given written instructions on home care and inspection of bandages. If possible, the nails/pads of the third and fourth distal phalanges should be left visible at the bottom of the bandage for monitoring. Owners can be asked to assess the apposition of the nails – when swelling occurs the nails will part or splay. Pressure bandages, if applied to stop haemorrhage, should be removed after 15 minutes to an hour. All other bandages should be reassessed within 24 hours to minimize the risks inherent in inadvertent misapplication of the bandage. Bandages placed on limbs with vascular injury or deep lacerations should be rechecked and changed frequently to monitor for increased tissue pressure due to oedema. Bandages should be checked at least twice daily by owners and changed every 2–5 days. If an animal shows signs of pain or excessive licking or chewing at the bandage, it should be removed as soon as possible.

Luxations

Traumatic luxations require definitive treatment as early as the systemic condition of the animal allows, in order to minimize cartilage destruction, muscle contracture and periarticular fibrosis. Examination under general anaesthesia and the use of two orthogonal radiographic views are essential to confirm the presence and direction of the luxation, concurrent periarticular injuries, and pre-existing disease such as hip dysplasia, which may influence management. There is likely to be damage to some part of the bone, muscle, tendon and ligament complex that confers stability on the normal joint. In some joints, surgical repair of this damage, coupled with postoperative support, is indicated to maintain reduction (Figure 17.19). The hip, elbow, temporomandibular joint and occasionally the shoulder have enough inherent stability to remain reduced despite some damage, and closed reduction of these joints is indicated as a primary treatment (Figure 17.20). Closed reduction should be performed as soon as possible after the injury occurs if the patient's condition allows safe anaesthesia. The Ehmer sling can be used to assist stability of the hip joint after reduction, and the Velpeau sling may be applied to support the shoulder (Figure 17.21).

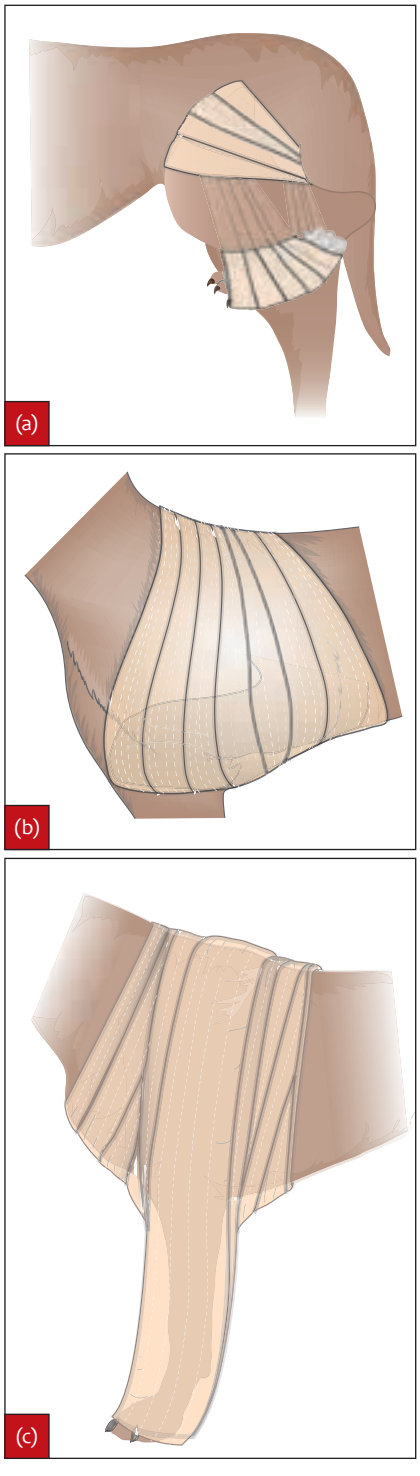
Affected joint	Direction of luxation	Technique for reduction (under general anaesthetic)	Postoperative support	Comments
Temporomandibular	Rostrodorsal	Lever in mouth and close mouth	Tape muzzle 7–10 days	Associated fractures may require surgery
	Coronoid displacement	Open mouth further and move mandible towards midline	None	Partial zygomatic arch resection if recurrent
Scapulohumeral	Medial	Manipulate proximal humerus/acromion	Velpeau 2–3 weeks (see Figure 17.21b)	Small dogs, often congenital
	Lateral	Manipulate proximal humerus/acromion	Spica	Large dogs, often traumatic
Elbow	Lateral	See Figure 17.20	Maintain extension	Very rarely medial. May need surgical reduction
Carpus	Variable	Surgical	Support bandage	Arthrodesis may be required if function is unsatisfactory
Phalangeal	Lateral or ablaxial	Closed for pet animals, surgical treatment in working dogs	Support bandage	Requires surgical imbrication of collaterals, or arthrodesis
Hip	Craniodorsal	See Figure 17.20	Ehmer sling or cage rest (see Figure 17.21a)	Surgical stabilization ultimately required in many cases (15–71%)
	Ventral	Externally rotate and abduct hip (and adduct stifles) whilst gently pushing dorsally. If reduction is unsuccessful and hip displaces craniodorsally, treat as in Figure 17.20	Hobble	Closed reduction usually successful
Stifle	Cranial	Surgical	Spica or ESF	Repair combination injuries of collaterals and cruciates
Tibiotarsal	Variable	Surgical	Bandage, splint or ESF	Repair fractured malleoli and collateral ligaments if possible

17.19 Management of luxations. ESF = external skeletal fixation.

Technique for elbow reduction:
1. Fully flex the elbow and abduct and pronate the antebrachium whilst applying medial pressure to the caudal ulna to engage the anconeus.
2. Extend the elbow slightly and then slowly extend the elbow further and pronate and adduct the antebrachium whilst applying medial pressure to the radial head.
3. Use the high support bandage or spica, to maintain extension, or carpal flexion bandage to avoid weight-bearing.

Technique for reduction of craniodorsal hip luxation:
1. Externally rotate the femur; distract the limb against countertraction.
2. Adduct then internally rotate, extend and abduct the limb.
3. Manipulate through the full range of movement to dispel clots.

17.20 Technique for reduction of elbow and hip luxations.



17.21 Bandaging the upper limb. (a) The Ehmer sling is a figure-of-eight bandage, which internally rotates the hip and prevents re-luxation. (b) The Velpeau sling provides stability for the shoulder area and prevents weight-bearing by limiting movement of the limb. (c) The spica splint stabilizes the elbow and humerus and can also be used on the hindlimb. The antebrachium is padded with a Robert Jones bandage and there is some padding over the scapula. A flat lateral splint is placed over the midline at the tip of the scapula and all the way down to the foot. The splint can be made from a sheet of thermosetting cast material and pleated for resistance to bending. It is held in place with adhesive tape over the Robert Jones dressing and a body bandage around the thorax.

In general, surgical reduction and repair of any joint should be considered if:

- Closed reduction is impossible
- The joint is still unstable or luxates easily after closed reduction
- Periarticular or articular fractures prevent reduction or require fixation
- Exploratory surgery is required to evaluate periarticular structures such as nerves
- Developmental or congenital abnormalities are present, which can cause continuing instability after reduction.

Articular fractures

Articular fractures should be treated definitively within 24–48 hours, provided the animal can be safely anaesthetized. Accurate reconstruction of articular surfaces, compression and rigid internal fixation are essential. Early return to function minimizes periarticular fibrosis and joint stiffness. Bandages or splints applied prior to treatment will be beneficial in decreasing swelling and increasing comfort, but are contraindicated in some situations. Cats in particular do not tolerate bandages well and, with closed injuries, cage rest may be preferable to bandaging. In general, the joints below the elbow and stifle can be supported with a bandage or splint. The elbow and stifle can be supported if necessary using a spica splint (see Figures 17.6h, 17.21c and 17.22a). Support of either the shoulder or hip joint prior to definitive treatment is generally not necessary, as the large muscle mass surrounding these joints provides sufficient support.

Diaphyseal fractures

Fractures involving the pelvis, scapula, femur and humerus should generally be left unbandaged. The muscle mass surrounding these bones provides some support, and bandages for these areas are cumbersome and restricting. Tubular bandages are ineffective in supporting these fractures and tend to form a pendulum of extra weight swinging at the level of the fracture. Femoral and humeral fractures may be supported with spica splints for transport or if repair must be delayed. Cage rest with suitable analgesia may be preferable. Fractures of the bones below the elbow and stifle should be supported with a bandage or splint. The combination of a splint and bandage (see Figure 17.6g) usually provides better stability to a fractured part than a bandage in isolation, even a well padded bandage.

Spinal fractures

Spinal fractures are candidates for immediate treatment, despite the high (40–50%) incidence of concurrent injury to thoracic or abdominal organs (Selcer *et al*., 1991). The potential for injury to the spinal cord itself is high and early intervention is essential to allow the maximum chance of conserving spinal cord function. There is a risk of further injury to the spinal cord during transport and examination of the patient. Animals should be transported on a flat board, a firm stretcher or slung in a strong blanket.

Examination: Early neurological examination is important, but extensive testing involving movement of the animal may cause further problems. Particular attention should be paid to whether deep pain sensation is present, and the testing of local reflexes, where all the muscle groups should be observed acting coherently. Repeated



17.22 Bandages in use on dogs. (a) Spica splint on a German Shepherd Dog after closed reduction of a lateral shoulder luxation. (b) Robert Jones dressing. (c) Carpal flexion bandage. (d) Hobbles placed on a dog while still anaesthetized after surgery.

monitoring is important to assess any change in status. Survey radiographs of the conscious patient are indicated, as sedation, muscle relaxation and positioning for radiographs may cause further damage at the site of instability. Lateral views of the entire spine are advisable as multiple fractures can occur. Oblique views assist evaluation of the articular processes and can be taken with the animal in lateral recumbency. Positioning for dorsoventral views can be hazardous, and a horizontal beam view is the preferred option (Wheeler and Sharp, 1994). Orthogonal views should be taken if the site of injury is not obvious on one view (Figure 17.23).

It is important to assess the stability of the fracture. Bending, shear, rotational and axial loading forces all act on the spine. Radiographic evaluation of the damaged areas can indicate the residual capacity of the spine to resist these forces, and indicate the optimum fixation technique. The key areas of evaluation are the ventral spinal component (i.e. the vertebral body and the intervertebral discs), which resists load and bending, and the articular processes, which resist a combination of forces. If one or both of these areas are severely compromised, the fracture will be unstable and a candidate for surgical fixation. More complex systems for staging the damage in relation to stability can be consulted, but the information is often difficult to apply to commonly occurring fracture patterns (Smith and Walter, 1985; Patterson and Smith, 1992; Shores, 1992). Stress radiography under fluoroscopy to evaluate instability should only be undertaken with



17.23 This cat presented with sudden-onset hindlimb paraparesis. Patellar reflexes were exaggerated and sciatic myotatic reflexes reduced. (a) Ventrodorsal radiograph of the cat's lumbar spine. There is a left ilial fracture. The unusual sacroiliac joint was considered to be an incidental finding. (b) Lateral radiograph showing a compression fracture of the body of the sixth lumbar vertebra.

extreme caution (Wheeler and Sharp, 1994). If available, advanced imaging techniques such as computed tomography (CT) and/or magnetic resonance imaging (MRI) are beneficial, providing more information about the fractures and also information on the integrity of the spinal cord (Johnson *et al*., 2012).

Treatment: Owners of animals that are being treated for spinal fractures need to commit themselves to a 4–6-week recovery period to allow an opportunity for return to function. Animals without deep pain sensation have a poor prognosis for any return to function. Although conservative and medical therapy coupled with continual reassessment, or exploratory surgery to identify a malacic cord, are possible in these patients, euthanasia should be considered.

The treatment of spinal fractures has three components: medical therapy; stabilization; and decompression (Figure 17.24). Selection of appropriate therapy is initially based on the clinical presentation.

Indications for conservative treatment are:

- Animals that can walk or are paraparetic
- Animals that exhibit strong voluntary movement and have peripheral pain perception
- Animals that have minimal pain or pain that can be controlled by drugs.

Major indications for surgery are:

- Non-ambulatory animals
- Palpably unstable or significantly displaced injuries
- Animals that deteriorate with conservative treatment
- Animals with peripheral pain perception but no voluntary movement
- When decompression is required for displaced spinal segments, bone fragments or extruded disc material
- Non-ambulatory animals with no deep pain
- Animals with significant pain associated with the fracture.

Medical management: Medical management includes appropriate analgesia once the neurological evaluation is complete. Acute injury to the spinal cord initiates a sequence of vascular, biochemical and inflammatory events that result in secondary tissue damage. Initial treatment should primarily focus on addressing the patient's cardiovascular and respiratory system. Supportive measures to restore systemic perfusion are vital to minimizing secondary injury (Park *et al*., 2012). In the longer term, analgesics, including opioids and non-steroidal drugs, together with confinement and immobilization are probably the mainstay of non-surgical management. High-dose methylprednisolone sodium succinate is falling out of favour because studies have shown little therapeutic benefit and severe adverse effects (Kube and Olby, 2008).

Stabilization: Stabilization can be carried out conservatively (Figure 17.25) or surgically depending on the clinical signs, radiographic indications of stability and anatomical position (see Figure 17.24). Early surgical intervention or decompression remains the best treatment option in managing acute compressive injuries in veterinary patients (Kube and Olby, 2008). If surgery is indicated, a myelogram, MRI or CT scan can be used to determine if there is a significant lesion that requires decompression; however, evaluation of the survey radiographs alone may be sufficient to deduce this information. Hemilaminectomy should be used for decompression as it has minimal effect on spinal stability. Decompression should always be accompanied by appropriate internal fixation to stabilize the injury.

Treatment	Indications	Advantages	Disadvantages
Cage rest. Confine in very small space until there is radiographic evidence of healing	Ambulatory or paraparetic animals with stable thoracolumbar injuries	Economical. No exposure to lengthy surgery and anaesthesia	Difficult to restrict some animals. Animals may suffer prolonged discomfort, and neurological deficits may worsen or even become irreversible
Back splinting (Patterson and Smith, 1992)	Caudal cervical, thoracic and lumbar injuries	Economical. Provides better stability than cage rest. Can combine with internal fixation	Intensive nursing required, especially for large dogs. Not ideal if ventral component involved
Vertebral body pinning	Lumbar fractures	Economical. Implants often readily available	Weakest form of internal fixation
Dorsal spinous process plating. Apply a metal or plastic plate to the dorsal spinous processes either side of the lesion	Thoracic and lumbar fractures	Effective combined with vertebral body plating in resisting bending forces	Difficult to apply to small dorsal spinous processes. Processes may fracture
Modified segmental fixation. Secure a pin or pins to two dorsal spinous processes cranial and caudal to the lesion	Thoracic and lumbar injuries in small dogs and cats	Economical. Equipment usually readily available	Articular processes may fracture. Immobilizes a long segment of the spine. Ideally requires intact ventral component
Vertebral body plating. Plate is applied to the dorsolateral vertebral bodies above the transverse processes	Thoracic and cranial lumbar vertebrae (application caudal to L3 requires sacrificing nerves to the lumbosacral plexus)	Effective *versus* bending forces, enhanced when combined with dorsal spinous plating. Can combine with hemilaminectomy	Difficult to apply plate in thoracic region as need to disarticulate ribs. Little resistance to rotational forces
Pins or screws and polymethylmethacrylate	Any location	Very versatile technique. Provides rotational stability	Occasionally see wound infection and pin migration
Trans-ilial pinning. Pin through the wings of the ilium dorsocaudal to the bone of the dorsal spinous process of L7	Lumbosacral injuries	Can combine with dorsal spinous body plating or stapling	Pins may migrate and may provide inadequate stability if used in isolation

17.24 Treatment options for spinal fractures and luxations.



17.25 Temporary neck splinting for an atlantoaxial subluxation fracture. The splint should extend from the mandible to the thorax. Careful monitoring is required; upper airway obstruction and inability to move the chest wall are common concerns.

Compartment syndrome

Acute compartment syndrome following trauma has been reported in the dog (De Haan and Beale, 1993). Bleeding or tissue swelling within a fascial compartment can cause a rapid rise in pressure in that compartment, which is responsible for the problem. The condition is common in humans, especially associated with tibial fractures. Due to the non-specific nature of the signs and the difficulty of making a definitive diagnosis, the condition may be underdiagnosed in the dog.

Pathogenesis

Physiological compartments are enclosed by skin, epimysium, fascia or bone. The term osseofascial is used to describe a compartment where bone and fascia are the barriers to swelling (Basinger *et al*., 1987). Extraneous material such as a dressing or a cast can also define a compartment. In dogs, osseofascial compartments have been reported in:

- Craniolateral crus
- Caudal crus
- Caudal antebrachium
- Femoral compartment (complex multifascial envelope).

If the pressure in one of these compartments rises, the veins will collapse and local venous pressure will rise. This reduces the arteriovenous gradient, blood flow and tissue perfusion, leading to ischaemia and necrosis. Peripheral nerves and muscles have limited resistance to hypoxia and are damaged first by the rise in pressure, leading to impaired neuromuscular function (Rorabeck and McGee, 1990). As there is an inverse linear relationship between pressure and the time taken for the tissue damage to become irreversible, early treatment is essential. Reperfusion injury, for example, after cast removal, may also play a part in the pathophysiology of the condition. Pressure can increase for several reasons:

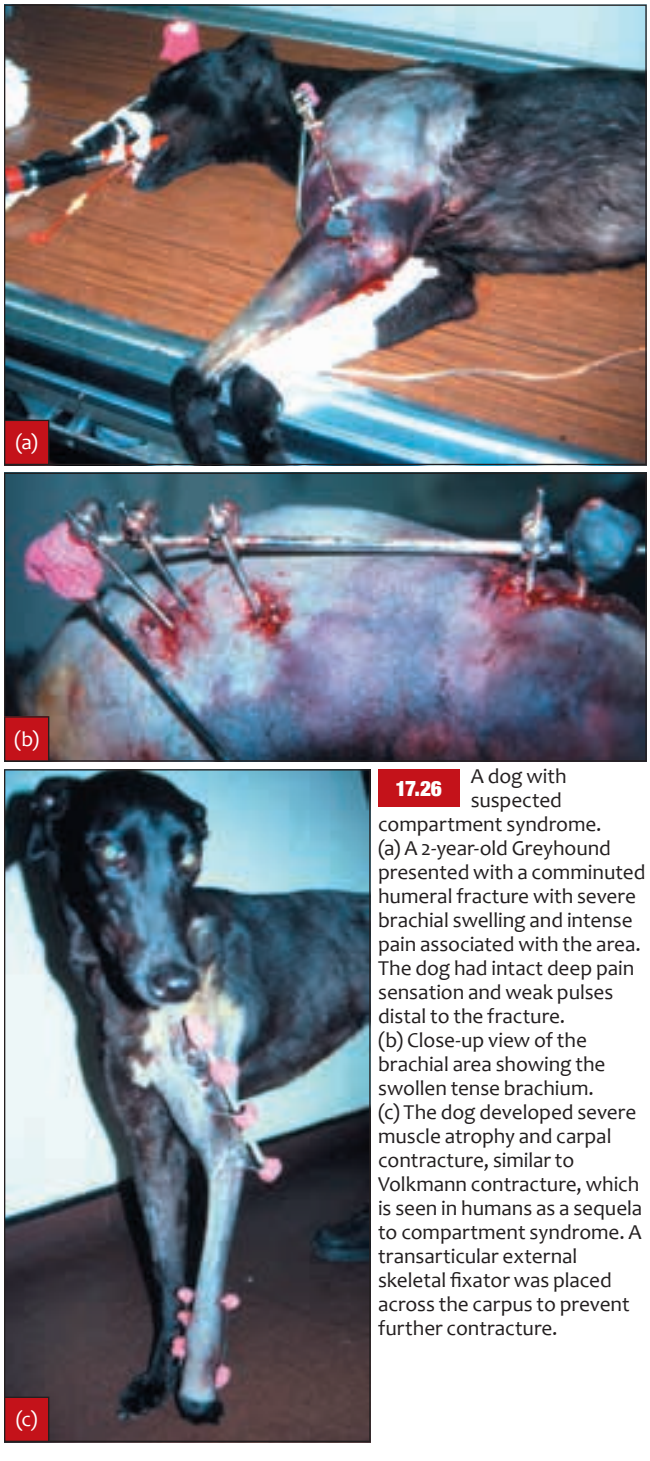
- Bleeding into the compartment after trauma
- Increased capillary permeability and swelling following ischaemia (reperfusion injury may occur here too)
- External pressure constricting a compartment, for example, a bandage.

Normal pressures in muscle average 4 mmHg, with a range of 0–8 mmHg. Measurements of muscle pressure in dogs with compartment syndrome reported in the literature were 26–30 mmHg (De Haan and Beale, 1993).

Diagnosis and treatment

Compartment syndrome should be considered in trauma patients with swollen and tense limbs, where there is little compliance to surface finger pressure and which are especially uncomfortable and resistant to analgesia (Figure 17.26). Arterial pulses are generally still palpable, as the pressure does not usually rise enough to stop arterial blood flow. There is decreased sensation due to nerve compression. It can be difficult to differentiate compartment syndrome from arterial occlusion and neuropraxia.

The only reliable method of diagnosis is to measure tissue pressures. Slit catheters, wick catheters, needle manometers and continuous infusion systems have been used to measure pressure. However, the simplest practical system is to use a standard central venous pressure



17.26 A dog with suspected compartment syndrome. (a) A 2-year-old Greyhound presented with a comminuted humeral fracture with severe brachial swelling and intense pain associated with the area. The dog had intact deep pain sensation and weak pulses distal to the fracture. (b) Close-up view of the brachial area showing the swollen tense brachium. (c) The dog developed severe muscle atrophy and carpal contracture, similar to Volkmann contracture, which is seen in humans as a sequela to compartment syndrome. A transarticular external skeletal fixator was placed across the carpus to prevent further contracture.

manometer linked to an ordinary needle and zeroed to atmospheric pressure; the tip of the needle is then placed into the compartment and the pressure measured.

Compartment syndrome should be treated as an emergency. Rapid relief of the pressure is necessary to prevent irreversible damage resulting from the hypoxia and ischaemia. For cases of confirmed or suspected compartment syndrome, the treatment is to remove the barrier to swelling by cutting the skin, fascia and epimysial layer. In humans, after fasciotomy the incision is left open for delayed closure or split skin grafting 7–8 days later, but postoperative management in animals is facilitated by closure of the skin (De Haan and Beale, 1993). Fractures concurrent to compartment syndrome should be rigidly fixated to promote soft tissue healing, but this can be delayed if necessary. Removal of dressings or bivalving casts can reduce compartment pressures by 50–85% and should be considered if there is a potential for compartment syndrome to occur. Untreated compartment syndrome causing prolonged muscle ischaemia can lead to muscle contracture, which may cause permanent disability in the animal and necessitate amputation.

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Chapter 18

Dermatological emergencies

Petra Roosje

Dermatological conditions in small animals are most often chronic problems that do not require emergency care. Some acute problems, although not life-threatening, may be alarming to the owner – for example, 'hot spots'. Other rare conditions, which may not appear severe initially, can eventually prove to be fatal to the animal, e.g. toxic epidermal necrolysis (TEN).

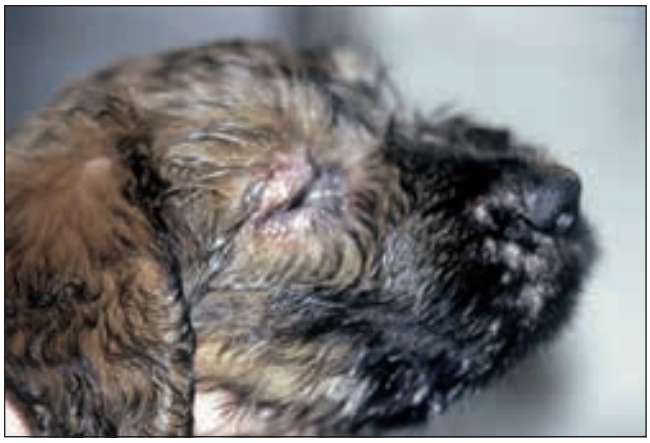
As some of the more serious skin diseases can be difficult to differentiate from each other on the basis of history, physical examination and basic clinicopathological testing, it is important to perform multiple skin biopsies of early lesions and also more developed lesions, and submit these specimens to a pathologist with a special interest in dermatology. It is imperative to obtain a precise history, including the description and evolution of lesions, and also of previous treatments and response to treatment. This chapter describes a selection of acute dermatological conditions, emphasizing those that may have serious consequences for the animal's health.

Juvenile cellulitis

Juvenile cellulitis (puppy strangles or juvenile pyoderma) is an uncommon disease that affects puppies between the ages of 3 weeks and 4 months. The condition has also been described rarely in adult dogs (Jeffers *et al*., 1995; Neuber *et al*., 2004). It can occur in any breed. Usually only one puppy is affected but occasionally several puppies within a litter are affected. The pathogenesis is unknown, but an immune dysfunction is suspected. A correlation with vaccinations has not been proven. Secondary infection with *Staphylococcus pseudintermedius* or other species may occur.

Clinical signs

Initially, affected puppies have a painful and swollen face. The eyelids, muzzle and lips are especially affected (Figure 18.1). Papules and pustules develop within a few days. The pinnae are also often involved and, occasionally, the preputial and perianal areas may be affected. Other findings commonly include enlarged mandibular and prescapular lymph nodes, which may become abscessed, rupture and drain in some cases. Lethargy, anorexia and fever occur in around 50% of the puppies. Small numbers of affected animals show joint pain. Occasional puppies may have a concurrent sterile pyogranulomatous panniculitis, preceding hypertrophic osteodystrophy (Wentzell, 2011) or hindlimb paresis (Park *et al*., 2010).



18.1 Briard puppy with swollen eyelids, nose and pinnae due to juvenile cellulitis.

Diagnosis

Differential diagnoses should include angioedema (in the early phase), staphylococcal pyoderma, demodicosis and cutaneous drug reaction. Multiple deep skin scrapings should be taken to exclude demodicosis. A thorough history will provide information about previous drug administration. Aspirates of intact lymph nodes and pustules should be taken for cytology and bacterial culture. Cytology of intact pustules will reveal pyogranulomatous inflammation without microorganisms. Bacterial cultures of intact pustules should be negative unless there is secondary staphylococcal infection. Skin biopsy specimens of early lesions show multiple discrete or confluent periadnexal granulomas and pyogranulomas consisting of macrophages and neutrophils.

Clinical management

Oral prednisolone (1.5–2 mg/kg/day) should be given until the clinical signs improve, usually within 1–2 weeks. Corticosteroid administration should then be tapered and stopped over 4–6 weeks. Typically, depressed puppies become livelier within 1–3 days after the first prednisolone administration but skin lesions respond more slowly. Ciclosporin (5 mg/kg/day) is effective in combination with prednisolone (Park *et al*., 2010). Concomitant administration of antibiotics is often indicated as secondary bacterial infection is common. Affected puppies generally do not recover with antibiotic therapy alone (White *et al*., 1989).

Cefalexin (40–60 mg/kg/day divided into two doses) is the drug of choice. Antiseptic washes, gels, soaks, wipes or shampoos containing 2–3% chlorhexidine have been recommended, but may cause struggling and stress in the puppy. If anorexia or fever is present, more intensive therapy is required, including intravenous fluid and electrolyte administration, blood glucose monitoring and glucose therapy. Euthanasia may be indicated in severe cases. The prognosis is generally good, although permanent facial scarring can occur.

Pyotraumatic dermatitis

Pyotraumatic dermatitis ('hot spots' or acute moist dermatitis) is a condition frequently seen in dogs and less often in cats. 'Hot spots' can occur at any age. The condition is most commonly reported in heavily coated breeds such as the Leonberger, Golden Retriever, German Shepherd Dog and Bernese Mountain Dog, but is also seen in Rottweilers and other breeds (Holm *et al*., 2004). In breeds with a dense coat, increased temperature and slow drying of the coat make the skin surface favourable to bacterial colonization and overgrowth. Many 'hot spots' are thought to occur as complications of one or more of the factors listed in Figure 18.2. These factors can induce the 'itch, lick or scratch' cycle that varies in intensity between individuals. Lesions may be induced within a few hours.

- Flea-bite hypersensitivity
- Otitis externa
- Atopic dermatitis
- Foreign bodies in the coat
- Food hypersensitivity
- Dirty, matted, unkempt coat
- Ectoparasite infestations
- Painful musculoskeletal disorders
- Anal sac problems

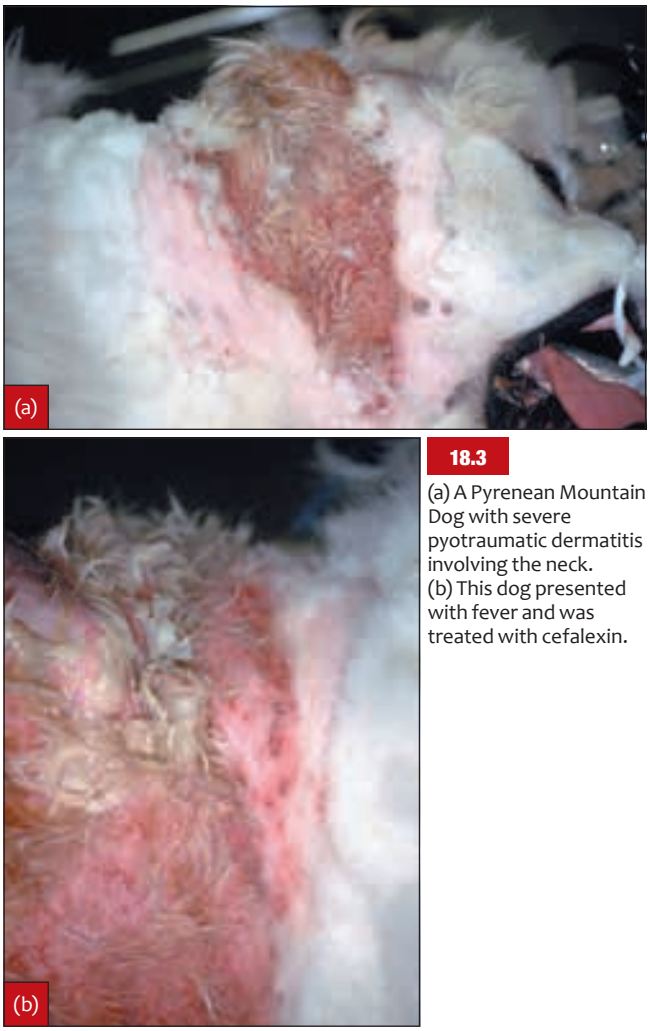
18.2 Causes of pyotraumatic lesions.

Clinical signs

These animals are presented with a history of acute onset of disease. The self-induced painful lesion consists of a well circumscribed area of moist matted hair, glued together with exudate (Figure 18.3). Predilection sites are the cheek, neck, lumbar region and flank.

Diagnosis

The diagnosis is based on the clinical appearance and a history of acute onset. The lesion usually occurs in an area where the dog can cause self-trauma. The primary cause may not always be apparent. Clinically it is hard to differentiate true pyotraumatic dermatitis from a pyotraumatic folliculitis. Moreover, pyotraumatic dermatitis lesions often have histological evidence of folliculitis (Holm *et al*., 2004). It may be, however, that folliculitis is a time-related effect. True pyotraumatic dermatitis is a superficial process consisting of a flat erosive or ulcerated lesion. The hair is lost from the lesion but a clear margin is present between the lesion and the normal surrounding skin. In pyotraumatic folliculitis, the lesion is thickened, plaque-like and surrounded by satellite papules and pustules. In most patients, hairs epilate easily from the inflamed area.



18.3 (a) A Pyrenean Mountain Dog with severe pyotraumatic dermatitis involving the neck. (b) This dog presented with fever and was treated with cefalexin.

Clinical management

The hair on and around the lesion should be clipped to allow a better examination of the lesion and thorough cleaning of the area. As this can be very painful for the dog, sedation or anaesthesia is usually needed. Initial cleaning with a chlorhexidine solution is recommended. In dogs with severe lesions, the owner should continue with daily rinsing or washing of the affected area followed by light towel drying of the area. Topical therapy containing a disinfectant or an antibiotic and a corticosteroid should be applied once or twice daily. Only products formulated as a gel or spray should be used.

In subacute cases or in the presence of folliculitis and furunculosis, oral cefalexin (40–60 mg/kg/day divided into two doses for at least 3 weeks) should be given. Initially, an Elizabethan collar, T-shirt or socks may be used to prevent further trauma to the lesion. Topical treatment should be continued until the lesion has dried, usually 7–10 days. Many dogs do not need oral corticosteroids, but if pruritus is persistent these patients may benefit from a short course of prednisolone (1 mg/kg/day for 3–5 days, then tapered). In case of recurrent lesions, possible causes for pyotraumatic dermatitis should be addressed. To prevent relapses in dogs with a dense coat and without an underlying cause (see Figure 18.2), clipping the whole body during the summer can be helpful if lesions occur primarily in summer.

Urticaria and angioedema

Immunologically mediated urticaria, angioedema and anaphylaxis can be thought of as the same disease, with variations in severity and target organ. Urticaria (hives) consists of focal superficial anaphylactic reactions visible as erythematous wheals. Possible causes are listed in Figure 18.4. Previous use of or contact with, for example, vaccines or drugs does not rule these out as a trigger, as urticaria may develop after multiple exposures to the drug or vaccine. Dogs are more commonly affected than cats. Urticaria lesions often disappear within a day but may persist longer, with development of new lesions. A chronic form also exists. The inciting cause of the wheal formation is often hard to identify. Wheals can be irritating to the animal and there is a risk that associated swelling of the mucous membranes may obstruct the airway. In angioedema, deep blood vessels are affected and the resulting oedema causes diffuse swelling; this is of particular concern if the airways are affected. Both urticaria and angioedema result from mast cell or basophil degranulation, which may have an immunological (type I hypersensitivity) or non-immunological origin.

- Foods
- Drugs
- Antisera, bacterins and vaccines
- Stinging and biting insects
- Hairs of processionary caterpillars[a]
- Blood transfusions
- Plants
- Intestinal parasites
- Infections[a]
- Sunlight[a]
- Excessive cold or heat[a]
- Oestrus[a]
- Atopy or allergic dermatitis
- Psychogenic factors[a]
- Vasculitis[a]

18.4 Factors reported to have caused urticaria in dogs and cats. [a]Reported in dogs only.
(Miller *et al.*, 2013)

Clinical signs

Urticaria can develop within a few hours. Lesions may be single or multiple and may occur all over the body (Figure 18.5). Animals are variably pruritic. Signs of angioedema consist typically of facial swelling and sometimes swelling of the extremities.



18.5 Dalmatian with urticaria showing multiple erythematous wheals.

Diagnosis

The differential diagnosis for urticaria includes folliculitis, erythema multiforme (EM), vasculitis and neoplasia. Definitive diagnosis is based on obtaining an extensive history and a thorough physical examination. Staphylococcal folliculitis can be mistaken for urticaria, especially in short-coated dogs, where hairs can stand out focally. In staphylococcal folliculitis lesions, hairs can be easily epilated and, compared with urticaria, lesions are more exudative. Clipping of the coat can help to identify lesions. Skin biopsy can be helpful for differentiation when the lesions persist. Vasculitis-induced lesions should not blanch upon pressure with a glass slide.

Clinical management

Therapy includes avoidance and elimination of the aetiological factors. In cases of urticaria, the wheals will resolve within a day unless exposure to the initiating factor continues or recurs. In this situation new lesions may continue to develop. Thus, it may be helpful to draw a line around wheals to monitor their development and assess if new lesions develop. If the animal is not distressed by the lesions and pruritus is minimal, therapy is not always necessary. It is important, however, to inform the owner of the risk of development of angioedema. The prognosis for angioedema varies with the severity and location. Angioedema of the larynx may produce potentially fatal airway obstruction.

In cases of pruritic urticaria, oral administration of prednisolone at 1 mg/kg/day for 1–2 days is often sufficient. Antihistamines are not always useful in acute urticaria but may help in preventing chronic urticaria; antihistamine treatment may need to be continued for several days. Identification and avoidance of the causative factor is the most successful long-term treatment. When there is life-threatening angioedema, dexamethasone (0.1–0.2 mg/kg i.v.) and diphenhydramine (2 mg/kg s.c.) should be given (see Chapter 14). The animal should be closely monitored for signs of respiratory distress (see Chapter 7). Anaphylaxis with associated hypotension is rarely encountered, but should be managed with intravenous fluids, supportive care, and possibly even additional treatment with adrenaline (epinephrine) (0.01–0.02 mg/kg i.v. or i.m.) while carefully monitoring the patient.

Cutaneous drug reactions

Drugs can induce various cutaneous adverse reactions with a wide range of clinical manifestations, which can mimic many other skin diseases (Figure 18.6). The severity of the lesions ranges from local, benign reactions to extensive skin lesions that may result in the death of the animal. Cutaneous drug reactions can occur as the result of immunological and non-immunological mechanisms. The latter may be due to overdosage, cumulative toxicity, genetic predisposition, interaction of drugs or idiosyncratic metabolism. These reactions can be evoked by any type of drug, including topically applied drugs, shampoos and insecticides. Although drug reactions occur in a very small number of patients, the incidence may be higher than is reported in the literature.

Clinical signs

Lesions can consist of urticaria, angioedema papules, erythematous macules, scales, erythema vesicles and

Drug or factor
Antibiotics: • Ampicillin • Cefalexin • Chloramphenicol • Ciprofloxacin • Co-amoxiclav • Enrofloxacin • Penicillin • Polymixin B • Sulphonamides • Tetracycline
Anti-epileptic drugs: • Primidone
Antifungal agents: • Griseofulvin • Itraconazole • Ketoconazole
Antiparasitic agents: • Diethylcarbamazine • Fenbendazole • Ivermectin • Levamisole • Combination of metaflumizone and amitraz • Moxidectin • Thiacetarsamide
Corticosteroids
Immunomodulators: • Aurothioglucose • Azathioprine • Chlorambucil • Cyclophosphamide • 5-Fluorocytosine • Hydroxyurea
Levothyroxine
D-Limonene
Methimazole
Non-steroidal anti-inflammatory drugs: • Carprofen • Firocoxib • Meloxicam • Metamizole
Propylthiouracil
Retinoids: • Isotretinoin
Blood transfusions
Antisera, bacterins and vaccines
Radiocontrast agents
Shampoos
Foods

18.6 Drugs or factors reported to cause dermatological adverse reactions in dogs and cats.
(Miller *et al.*, 2013)

bullae, or ulcerations. Draining nodular lesions, focal or diffuse alopecia, fixed drug eruptions (focal to multifocal sharply demarcated erythematous lesions) and pseudolymphomatous changes can also be seen (Affolter and von Tscharner, 1993). Diseases that can be caused by drug reactions include vasculopathies/vasculitis, panniculitis, drug-induced pemphigus foliaceus, bullous pemphigoid, superficial suppurative necrolytic dermatitis of Miniature Schnauzers, eosinophilic dermatitis, EM, Stevens–Johnson syndrome/toxic epidermal necrolysis (SJS/TEN), and acute febrile neutrophilic dermatosis (Sweet's syndrome). Signs of systemic illness can accompany the cutaneous signs.

Diagnosis

In addition to an extensive history and complete physical examination, other skin diseases should be excluded by means of multiple skin scrapings, bacterial culture, fungal culture and cytology. Skin biopsies may help to define a specific cause for the animal's lesions, may reduce the list of differential diagnoses, and can strongly support the diagnosis of a drug reaction. They may diagnose specific syndromes. As some dermatological drug reactions are life-threatening and can cause rapid deterioration of the patient, it is important to take biopsy specimens as early as possible, and request an urgent evaluation by a dermatopathologist. It is important to perform multiple skin biopsies at different lesion sites at different stages of development, or at sites bordering an ulcerated area. Disease-specific histopathological changes are sometimes apparent in a few lesions only. Although a histological pattern is not always pathognomonic for a drug reaction, the knowledge that a drug reaction can be the cause of the cutaneous lesions should lead to a careful review of the patient's history. The following list may help in making a tentative diagnosis of a drug reaction:

- When a skin condition worsens suddenly and unexpectedly after initiating drug therapy, or when there is a sudden deterioration after an initial improvement
- When skin lesions occur during drug treatment for a non-dermatological condition
- When observed manifestations do not resemble known pharmacological actions of the drugs
- When there is a history of previous exposure to the drug or related drugs, although prior exposure to the drug may have been tolerated without adverse effects
- When biopsy specimen examination results indicate histological features that can be consistent with a drug eruption
- When a physical examination demonstrates clinical signs consistent with a drug eruption and the animal received a drug known to cause skin reactions
- When resolution of the signs occurs following withdrawal of the drug. This may take 1–2 weeks and is dependent on the severity of the initial skin lesions and the presence of secondary infections
- When there is a negative challenge with other concurrently used drugs and the appropriate elimination of other causes.

The ultimate test of a causative association is to challenge with the suspect drug. This is not without serious risk, however, and is generally not recommended.

Clinical management

The most important part of the therapy is to discontinue the suspect causative drug and prevent further administration. When animals are receiving several drugs (including topical medication or shampoos) they should all be discontinued at the same time. If this is not possible, the drugs that were added to the regimen last should be stopped first. Most drug reactions improve spontaneously within 7–14 days upon drug withdrawal. Complete healing may take longer and depends on the severity of the skin lesions. Reactions due to repositol or body-stored agents (e.g. gold salts) respond more slowly after the drug has been withdrawn, and can continue for long periods.

Supportive therapy is not necessary unless animals have a more severe form of drug reaction such as SJS/TEN. If lesions have healed but animals are pruritic because of remaining crusts, a mild shampoo can be used. The choice of shampoo should be based on history of previous use. If the suspected causative agent was a sulpha-containing drug it may be safer to avoid use of a shampoo containing salicylic acid (Noli *et al*., 1995).

To prevent future drug reactions, it is important to inform the owner about the causative agent if known. Patients allergic to penicillins should not be treated with any other drug from the penicillin group.

Erythema multiforme and Stevens–Johnson syndrome/ toxic epidermal necrolysis

EM, SJS and TEN are rare diseases. Clinically, severe cases of EM, SJS and TEN can be hard to differentiate from each other in dogs and cats.

In humans, SJS and TEN are now considered to be one disease, with the only difference being the extent of the body surface area affected. Association with certain human leukocyte antigen (HLA) alleles has been demonstrated (Lee and Chung, 2013). Certain drugs may bind directly to the HLA complex and facilitate the development of self-reactivity and initiate cytotoxic signals (Lee and Chung, 2013). Although the pathogenesis is unknown in dogs and cats, a similar pathomechanism may apply.

EM, however, is a distinct disease with a different aetiology and is primarily associated with herpesvirus infections and less often with drug administration in humans (Sokumbi and Wetter, 2012).

A retrospective study demonstrated an absence of drug history in dogs with EM, and indications of a drug reaction in SJS, SJS–TEN overlap syndrome and TEN (Hinn *et al*., 1998). Other reports, however, have suggested an association of EM with a drug history in cats and dogs (Affolter and von Tscharner, 1993; Scott and Miller, 1999). One report even described an association with food substances (Itoh *et al*., 2006). In cats, EM has been reported to occur with herpesvirus infections (Olivry *et al*., 1999). Infection with parvovirus was demonstrated in dogs with EM (Favrot *et al*., 2000; Woldemeskel *et al*., 2011).

Erythema multiforme

Clinical signs

Lesions are variable but are initially characterized by acute onset of symmetrical erythematous macules or papules that spread peripherally and clear centrally, producing typical annular lesions (target lesions) or arciform patterns. Target lesions are defined as three zones of colour: an erythematous centre, and a paler ring followed by another erythematous ring (Figure 18.7).

Urticarial plaques, vesicles and bullae or a combination of lesions may be seen. Later in the course of the disease, the epidermis sloughs and erosions and ulcerations appear. Mucosal lesions consist of vesicles, bullae and ulceration. Animals may have cutaneous pain. Some animals may have a positive Nikolsky's sign, which is elicited by applying pressure with a blunt object like a pencil on a vesicle or to the edge of an ulcer, erosion or normal skin. The Nikolsky's sign is positive when the outer layer of the skin (epidermis) is easily rubbed off or pushed away, indicating poor cell cohesion. In dogs, the ventrum, mucocutaneous junctions, oral cavity, pinnae and footpads are often affected. In cats, lesions are most commonly seen on the trunk, oral cavity and mucocutaneous junctions. The mild form of EM can run a short course with less extensive skin lesions and without involvement of mucocutaneous junctions.



18.7 Target lesions in a dog with erythema multiforme. The causative drug was not identified because the dog had received multiple drug therapy.

Diagnosis

The diagnosis of EM is based upon history, clinical features, indication of a previous or concurrent viral infection, exclusion of other diseases (including neoplasia) and histopathology of multiple skin biopsy specimens. The list of differential diagnoses includes bacterial folliculitis, dermatophytosis, demodicosis, urticaria, vasculitis, paraneoplastic pemphigus, acute neutrophilic dermatitis, SJS, SJS–TEN overlap syndrome, TEN and autoimmune diseases. Clinical differentiation between EM, SJS, SJS–TEN overlap syndrome and TEN is currently based on an adapted clinical classification for dogs (Hinn *et al*., 1998) (Figure 18.8). Target lesions (see Figure 18.7) are typical lesions of EM in humans but are often not detected in dogs or cats with EM. In contrast, loss of epidermal attachment over a larger body surface area is typical of SJS–TEN in humans. The diagnosis of SJS might be more appropriate in animals with severe and extensive ulceration and a drug history. A diagnosis of EM is often based primarily on the histological changes of interface dermatitis and apoptosis of keratinocytes with lymphocyte satellitosis. Polymerase chain reaction (PCR) testing on skin biopsy samples for viruses (i.e. parvovirus and herpesvirus) is helpful for diagnosis of the underlying cause. An elimination diet should have been attempted before the diagnosis of idiopathic EM is made.

Clinical lesions	EM	SJS	TEN
Flat or raised, target or polycyclic lesions	Yes	No	No
Number of mucosal surfaces involved	0 or >1	>1	>1
Erythema, purpuric, macular or patchy eruption (% total body surface area (TBSA))	<50	>50	>50
Epidermal detachment (%TBSA)	<10	<10	>30

18.8 Abbreviated version of the clinical classification of erythema multiforme (EM), Stevens–Johnson Syndrome (SJS) and toxic epidermal necrolysis (TEN).
(Hinn *et al*., 1998)

Of note, if the disease is initially recognized at an early stage, the lesions may still progress. Additionally, it is important to look carefully at all mucosae and the whole body to ensure that the extent of the disease is not underestimated. Multifocal careful clipping of small areas is helpful for assessment.

Clinical management

The disease may be mild with spontaneous regression of lesions within a few weeks. A severe form may develop with extensive lesions demanding intensive and supportive therapy as discussed below for SJS and TEN. If extensive vesiculobullous lesions or ulceration are present, the prognosis is guarded. It is of great importance to try to identify an underlying cause and treat accordingly. The use of glucocorticoids is controversial. In severe cases, anecdotal reports suggest that ciclosporin (5 mg/kg/day) and pentoxifylline (25 mg/kg q12h) are helpful (Miller *et al*., 2013). Purified human intravenous immunoglobulin (IVIG) treatment was reported to be effective in some severe cases (Byrne and Giger, 2002; Nuttall and Malham, 2004).

Stevens–Johnson syndrome/toxic epidermal necrolysis

Clinical signs

Many animals have an acute onset of fever, anorexia and depression with development of generalized erythematous macules and patches. Vesiculobullous lesions may be present, which have a very short lifespan, and may progress to epidermal sloughing and ulceration within hours (Figure 18.9). Ulcerative lesions can involve oral mucosa, other mucosa and often footpads. These patients often have cutaneous pain and show a positive Nikolsky's sign.



18.9 Ulcerative lesions of toxic epidermal necrolysis due to a trimethroprim/sulfadiazine reaction.

Diagnosis

The differential diagnoses include burns, autoimmune diseases, EM, vasculitis, acute neutrophilic dermatitis and epitheliotropic lymphoma. Clinical differentiation between EM and SJS/TEN is based on the adapted clinical classification for dogs (Hinn *et al*., 1998) (see Figure 18.8). For histopathology, it is important to perform multiple biopsies of areas with different degrees of erythema and adjacent to ulcerations.

Histopathology will show hydropic degeneration of basal epidermal cells, full-thickness coagulation of the epidermis and typically minimal dermal inflammation ('silent dermis').

Unfortunately, there is often an overlap between the histological changes in severe EM, SJS and TEN. A definitive diagnosis is based on clinical signs, history and compatible histopathological findings.

Clinical management

The treatment of SJS/TEN includes elimination of the underlying cause and symptomatic and supportive measures. These animals may lose a considerable part of the epidermis. Fluids, electrolytes and proteins are lost and secondary bacterial infections or hospital-acquired infections occur. It is therefore imperative to handle these patients with the utmost care and keep their surroundings as clean as possible to prevent secondary bacterial infections and especially hospital-acquired infections (e.g. antibiotic-resistant pathogens). One study reported that the success of management of patients with TEN may increase when they are not bathed or clipped (Reedy *et al*., 1997).

In addition to the skin, other organ systems may become involved during the course of the disease. Blood and urine samples should be collected to establish baseline values. Oedema may develop and many animals succumb to the development of secondary factors such as shock, sepsis or disseminated intravascular coagulation (DIC).

As well as supportive intravenous fluid administration and pain management, antibiotics are indicated to address secondary bacterial infections, the choice being based upon earlier drug administration. The benefit of corticosteroid administration in these cases is controversial and the response may be poor. SJS, SJS–TEN overlap and TEN in humans are often treated with intravenous administration of purified human IVIG. Successful treatment with IVIG was reported in a dog with SJS, a dog with TEN and a cat with severe EM (Byrne and Giger, 2002; Nuttall and Malham, 2004). IVIG should be administered slowly over 6–8 hours at a recommended dosage of 0.5–1 g/kg (Hohenhaus, 2005). The same dose can be repeated on the following day. Ciclosporin is commonly used in human SJS/TEN patients and is also recommended in veterinary patients (5–7 mg/kg/day (dogs) or 7–10 mg/kg/day (cats)).

The prognosis is generally guarded or poor, with many owners electing for euthanasia. In humans, the extent of the skin lesions gives an indication of the prognosis. This may apply to animals as well.

Vasculitis

Vasculitis is a cutaneous reaction pattern and is associated with various diseases. Different vascular syndromes are associated with different diseases, clinical outcomes and specific histopathological features. Some animals may only present with skin disease whereas others have a variety of signs associated with systemic disease. Multiple causes have been described, including many different infectious diseases (e.g. *Leishmania* spp., *Rickettsia* spp., *Angiostrongylus vasorum*, *Dirofilaria immitis*), autoimmune diseases (e.g. systemic lupus erythematosus), immune-mediated diseases and adverse drug reactions (Swann *et al*., 2015).

Clinical signs

Dermatological lesions include erythema, erythematous macules, petechiae, ecchymoses, well defined ulcerations, oedema and a wide range of systemic signs associated

with vascular damage (Figure 18.10). Severity of the diseases associated with vasculitis varies from a mild disease to death. Clinical signs may be mild at presentation but can deteriorate very rapidly. DIC may occur.

Diagnosis

Diagnosis is based on histology. Specific histological features may indicate specific syndromes that are associated with certain diseases. Where appropriate, a full medical work-up to identify an underlying disease should be performed. Unfortunately, it is often difficult to find the underlying cause and thus a diagnosis of idiopathic (primary) vasculitis is made.

Clinical management

The underlying cause should be treated or eliminated when possible. In the case of more severe clinical signs, intensive care is needed. If no underlying cause can be found, treatment is primarily directed at supportive care, prevention of secondary bacterial infection and immunomodulatory treatment.



18.10 Pinna of a dog with multiple ulcerations due to vasculitis.

Primary irritant contact dermatitis

Irritant material coming into contact with animal skin can cause irritant dermatitis (Figure 18.11). The mechanism by which the epidermal cells are affected varies with the substance. Irritant dermatitis is therefore a heterogeneous disease with variable clinical manifestations.

A thorough history may give an insight as to whether any irritant substances were used on the animal or whether there are possible agents in the environment that could cause irritant dermatitis. The location of the lesion should fit with possible contact with the agent.

- Soaps
- Insecticides
- Topical fungicides
- Shampoos
- Disinfectants
- Flea collars
- Spot-on preparations
- Tar
- Caustic substances
- Plant-derived substances (tea tree oil, limonene)

18.11 Substances that may cause irritant contact dermatitis.

Clinical signs

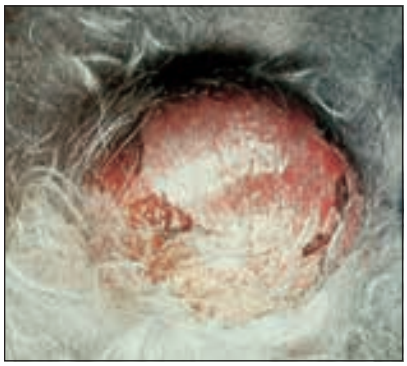
Environmental irritants typically produce lesions where the hair coat is thin or missing and where the body parts have contact with the irritant. Susceptible areas are the abdomen, thorax, interdigital spaces, legs, axillae, scrotum and flank (Figure 18.12). Oral lesions can occur when the animal has licked the primary skin lesion. When the offending agent is a liquid or a collar, the skin lesions occur where the substance touched the skin. Erythema or papules are primary lesions. In more chronic cases, erosions, crusts, lichenification or ulceration may occur. Pruritus may occur and can influence the appearance of the primary lesions.

Diagnosis

A careful history and physical examination may lead to a tentative diagnosis. When the irritants are less toxic, obtaining a definitive diagnosis is more difficult. The differential diagnoses should include atopic dermatitis, adverse food reaction, allergic contact dermatitis, *Malassezia* dermatitis, drug hypersensitivity and ectoparasite infestations.

Clinical management

The causative agent should be removed and further contact avoided. Washing of the animal may help to dilute or eliminate the agent. Greasy products might be best treated first by application of vegetable oil before washing the animal with a shampoo. If the dog or cat tries to lick or bite at the lesion, an Elizabethan collar or bandaging of the affected area may help. With removal of the agent the lesions should heal spontaneously. When animals are very pruritic, oral prednisolone at 1 mg/kg/day until the pruritus has stopped may be indicated.



18.12 Erythema and crusts due to an irritant contact dermatitis.

Canine uveodermatological syndrome

This syndrome occurs in many breeds but is most often seen in Arctic breeds such as Huskies, Samoyeds, Malamutes or Akita Inus. Acute clinical signs consist of uveitis with depigmentation primarily of the nasal planum, eyelids and lips. The skin changes usually occur simultaneously with or shortly after the ocular signs (see Chapter 10). Leucoderma (non-pigmented skin) and leucotrichia (white hairs) develop in the more chronic phase and can become widespread. Although the exact pathogenesis is unknown, in humans it is considered to be an autoimmune-mediated disease in which melanocytes are the immunological target.

Clinical signs

In dogs, the syndrome is characterized by acute onset of uveitis and/or depigmentation of the iris. Dermatological signs may occur concurrently with, or subsequent to, the ophthalmological problems and include depigmentation of the nasal planum, eyelids or mouth and erosive, crusting lesions around the eyes, muzzle and ears (Figure 18.13a).

Diagnosis

After a thorough history and physical examination, multiple skin biopsies should be performed. Differential diagnoses include pemphigus foliaceus, discoid lupus erythematosus, leishmaniosis, epitheliotropic lymphoma and vitiligo. Histopathology will reveal a band-like inflammation consisting of many macrophages with fewer plasma cells, lymphocytes and neutrophils. Macrophages often contain melanin (Gross *et al*., 2005).

Clinical management

Dogs with this disease are in fact ophthalmological emergency patients and not necessarily dermatological emergency patients. Treatment of ocular pathology is required to prevent the development of a panuveitis and possible blindness (see Chapter 10). Ophthalmic examinations should be periodically performed even when the cutaneous changes are in remission. The skin lesions are treated with a combination of azathioprine (1–2 mg/kg/day) and prednisolone (2 mg/kg/day). Oral ciclosporin is also reported to be effective (Blackwood *et al*., 2011). Initial haematology is indicated to facilitate monitoring for azathioprine-induced bone marrow depression. Generally, azathioprine should be given at the above dosage for at least a month or until lesions have resolved, whereas prednisolone may be tapered to an alternate-day regimen after 1–2 weeks, depending on effect. Monthly rechecks and repeat haematology should be scheduled. Unfortunately, many of these animals require lifelong treatment and it is therefore important to try to taper the medication to the lowest effective dose. Where animals respond to lower doses of treatment drugs, the prognosis for the dermatological changes is usually good, with repigmentation often occurring, although leucotrichia may remain (Figure 18.13b).



18.13 (a) Depigmentation of the nasal planum, perinasal and periocular erosions and erythema. (b) Repigmentation of the nasal planum and leucotrichia after 4 months of therapy with azathioprine and prednisolone.

Acquired feline skin fragility

These cats may be presented with freshly torn skin at one or more body sites (Figure 18.14). Tearing may also occur while handling the cat. Tearing occurs due to extreme fragility of the skin associated with very thin collagen fibres.

Clinical signs

The skin in these cats is very thin and atrophic, and often blood vessels are visible. The skin is not hyperextensible. Most cats with skin fragility have clinical signs of systemic disease caused by hyperadrenocorticism (spontaneous or iatrogenic), diabetes mellitus (mostly associated with hyperadrenocorticism), or possibly liver disease. In some cats no underlying disease can be found.



18.14 Avulsed skin in a cat with acquired skin fragility.

Diagnosis

Major differential diagnoses are indicative of different congenital connective tissue disorders. Chronic or topical use of corticosteroids or progestogens can induce skin fragility. Focal skin fragility should be discerned from generalized skin fragility. Investigations should be focused on finding the underlying cause. Histopathology may help to differentiate between a collagen disorder and acquired skin fragility.

Clinical management

The prognosis is guarded to poor as handling these cats can cause additional tearing. Spontaneous recovery is possible when the underlying disease is treated or corticosteroids are stopped.

Burns

Burns may result from radiation therapy, microwave radiation, and thermal or chemical insult to the skin. Thermal burns may result from the use of fires, heating pads/lamps, hair dryers, improperly grounded electrosurgical units (Figure 18.15), boiling water or oil. Chemical burns may result from contact with caustic or acidic materials.

Burns are classified according to their depth.

- Superficial partial-thickness burns affect only the epidermis, which becomes thickened and erythematous and ultimately desquamates. The burn



18.15 A dog with a full-thickness necrosis of the axilla due to an improperly grounded surgical unit.

usually heals by re-epithelialization in 3–6 days, and hair regrowth is likely.
- Deep partial-thickness burns involve the epidermis and part of the dermis. In these cases a marked subcutaneous oedema and inflammatory response occur. These burns heal by re-epithelialization from the remnants of hair follicles and sebaceous glands and from the wound edge. Healing rate and quantity of hair regrowth depend on the depth of the burn.
- In full-thickness burns, destruction of all cutaneous structures occurs and a dark brown insensitive leathery covering (eschar) is formed. After removal or sloughing of the eschar these wounds heal slowly by contraction and re-epithelialization. Hair regrowth will not occur and full-thickness burns often need surgical intervention.

Burn wounds may not only cause local tissue damage but can also cause severe systemic pathology. The respiratory system should be carefully evaluated in case of concurrent smoke inhalation (see Chapter 7). Burn patients exhibiting clinical signs of shock require intensive aggressive therapy, including management of fluid and electrolyte balance and body temperature. Due to increases in metabolic demand, a nutritious, high-calorie, high-protein diet should be fed if liver and kidney function are adequate. Monitoring of vital signs, mental status, bodyweight and urine output should occur throughout treatment. Pain management should be an integral part of the treatment. The minimum database should include a complete blood count, chemistry screen, urinalysis and blood gases (where available). Depending on the total body surface area (TBSA) involved, secondary bacterial infection is common due to tissue necrosis and loss of barrier function. This can lead to life-threatening sepsis.

Clinical signs

Burns in haired areas caused by microwave radiation, electric currents, chemicals, heating pads or cage dryers may not be obvious to the owner for a few days after the injury. Well demarcated erythema occurs initially, and the lesions often feel hard and dry. This stage is followed by development of adherent crusts, erosions or the odour of necrosis. The shape of the lesion (angular borders, 'drip pattern' or symmetry) may suggest the origin of the burn.

Burns caused by hot metals or fire are usually immediately obvious but it may take 24–48 hours before the full extent of the lesion is visible. Chemical burns are erosive and necrotic in nature and it can take 24–48 hours before their maximum extent is seen.

Diagnosis

The diagnosis is clear when the burn incident has been observed, but may be less so if it is not, especially when the burn is superficial. A complete history and physical examination, including eyes, ears, oral cavity, respiratory tract, urogenital tract, anus and footpads, should be performed. The presence of circulatory shock and/or respiratory thermal injury should be assessed and treated. Biopsy specimens of different parts of the lesion (especially the margins) can be helpful to discern between chemical or thermal burns and electrical burns.

Clinical management of thermal wounds

If an owner calls immediately after a burn due to hot water or a chemical substance, the best immediate therapy is to rinse the site with cold tap water for at least 10 minutes. Identification of the chemical substance is useful for choosing a neutralizing agent that can be applied after lavage. The depth and the extent of the burn (percentage of TBSA) should be assessed. A decision should be made whether:

- The thermal injury is minor, requiring only local therapy
- Local wound care and systemic therapy are indicated
- The animal is burnt to such an extent that euthanasia is indicated. Euthanasia should be considered when full-thickness burns cover more than 30–50% of the TBSA or when there are severe burns of the face or genitalia with a chance of permanent deformity (Swaim and Henderson, 1997).

Extensive burns generate extensive costs and this should be communicated to the owner at an early stage.

Evaluation of the depth of a burn may be difficult in the early stages following injury. If hair is still present and epilates easily, it generally indicates a deep burn. Analgesia should be provided, and the patient may be sedated to facilitate treatment, although care should be taken if ventilatory or cardiovascular function is compromised. Hair should be clipped carefully from the burned surface. If the burn has just occurred, application of saline or water (3–17°C) for at least 30 minutes may relieve pain and arrest the progression of the burn. When large burns are present, care should be taken to avoid hypothermia.

The following procedures should be considered:

- Moist wound healing is preferred
- In the first days after a burn injury the wound produces exudate, and a primary absorptive bandage (e.g. paraffin gauze) should be used. After this stage the wound is usually drier and a non-adherent occlusive type or hydrocolloid dressing should be used under the bandage. Wounds should always be handled with gloves to minimize the risk of further infection
- To help soften and separate viable from non-viable tissue in superficial and deep partial-thickness burns, the wound can be gently spray lavaged with warm saline in between bandage changes. Necrotic tissue can be debrided from the wound after the lavage. In contaminated wounds a topical antimicrobial can be used for a few days after wound cleansing. Between lavages, low-adherence dressings should be applied
- Superficial partial-thickness burns can be allowed to heal as an open wound
- In deep partial-thickness burns, the resulting wound can be allowed to heal by contraction and

re-epithelialization with regular bandage changes and systemic medication. Wound healing is supported by a moist environment. Alternatively, a combination of reconstructive techniques and healing as an open wound may be used
- In full-thickness burns with areas of demarcated devitalized tissue, the tissue can be debrided by wound excision and eschar removal. An eschar may protect the underlying tissue from electrolyte, fluid and protein loss, but it can also harbour bacteria and influence wound contraction. Total removal of the eschar is indicated when the animal is stable enough for anaesthesia
- When all of the devitalized tissue has been removed from a full-thickness burn, it may be possible to close the wound by relocation of local tissue using a skin flap
- Consultation with specialists is advised for animals with extensive lesions or systemic signs.

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Chapter 19

Toxicological emergencies

Jonathan M. Babyak and Justine A. Lee

The iconic skull and crossbones symbol is universally recognized as a warning of a substance's potential for causing harm. This simple representation of death accurately embodies our innate fear of poison. The word 'toxicity' refers to a poison's inherent ability to cause toxicosis. Toxicosis refers to the disease state caused by a toxic substance.

Toxicants are substances that have the potential to be toxic and are generally man-made. Although commonly used to refer to all substances with toxic potential, toxins are biologically derived substances that usually have high complexity and molecular weight. This is contrasted with poisons, which are less complex compounds of non-biological origin. A glossary of common terms used in toxicology can be found in Figure 19.1.

Exposure to a toxicant is common in veterinary medicine due to the accessibility of toxicants in the home and outdoor environment, and the inherent curiosity of dogs and cats. Veterinary patients are often exposed to common food items, over-the-counter (OTC) and prescription medications, poisons 'under the kitchen sink' and toxicants readily accessible in the garage or shed. This chapter focuses on preventing and ameliorating the harmful effects of toxicants in veterinary patients, reviews triage and stabilization of the poisoned patient, and provides information on obtaining an appropriate toxicological history, decontamination, appropriate use of activated charcoal, and overall symptomatic and supportive care of the poisoned patient. Specific common toxicants are also reviewed.

For further detail, a toxicology-specific resource is recommended. Overall, with rapid identification of the toxicant, treatment and supportive care, the prognosis for the poisoned patient is generally excellent.

Term	Abbreviation	Definition
Toxicant		A toxic compound, typically a result of human activity
Toxin		High molecular weight, complex, biologically derived compound
Poison		Low molecular weight, less complex, non-biologically derived compound or chemical
Toxicity		Describes the degree to which a compound is capable of causing toxic effects
Toxicosis		Disease state caused by a toxin or poison
Lethal dose	LD, LD_{50}	Reports the dose that is lethal; LD_{50} is the dose at which the mortality is 50%
Half-life	$T_{1/2}$	Time required for 50% of a compound to undergo a defined function (e.g. excretion)
Volume of distribution	V_d	Relates plasma concentration to total body concentration once equilibrium has been reached
Bioavailability	F	Percentage of a substance available to be processed by the body

19.1 Common terms and abbreviations used in toxicology.

Triage and stabilization

With a poisoned patient, special attention should be paid to ensuring appropriate triage and assessment, with a focus on the respiratory, cardiovascular and neurological systems (e.g. airway, breathing, circulation, dysfunction; the 'ABCDs'). Emergency treatment should be administered to restore adequate ventilation and oxygenation, maintain cardiovascular function and adequate tissue perfusion, treat neurological disturbances, stabilize core body temperature, and correct electrolyte and acid–base disturbances. If a specific toxicant has already been determined, an antidote may be appropriate to correct or prevent life-threatening clinical signs (e.g. naloxone for opioid overdose, fomepizole for ethylene glycol), if available.

History

Once a patient has been stabilized, a specific toxicological history should be obtained. The owner should be questioned carefully to help confirm the suspected toxicant and formulation (e.g. sustained- or extended-release product). Identifying an active ingredient (AI) and dose will allow the veterinary surgeon (veterinarian) to determine the risk of toxicosis. A poisoned patient, even if it appears stable, should never be left waiting, as the window for maximum efficacy of decontamination may pass. The owner should also be questioned as to whether there has been an attempt at inducing emesis and, if so, what agent was used. Additional important questions to include as part of a thorough toxicology history are found in Figure 19.2, while Figure 19.3 provides recommendations for phone-based triage.

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Questions to ask pet owners on presentation

1. What was the product ingested? Do you know the active ingredient?
2. Did you give your pet anything at home (e.g. washing soda, hydrogen peroxide, milk) when you found that it had been poisoned?
3. How many tablets could have been ingested in total? What was the minimum and maximum amount that your pet could have been exposed to?
4. Was it an extended, long acting or sustained-release product? Was there an extra 'letter' after the brand name (e.g. Claritin *versus* Claritin-D, Advil *versus* Advil-PM)?
5. When did your pet have access to the product?
6. Has your pet shown any clinical signs yet?

19.2 The owners of a poisoned pet must be questioned carefully so that the veterinary surgeon can move forward with appropriate and directed treatment.

Telephone triage advice

- Safely remove the pet from the area of poisoning so additional ingestion does not occur
- **Do not** give any home remedies found on the Internet (e.g. milk, peanut butter, oil, fat, salt)
- **Do not** induce emesis without consulting a veterinary surgeon or an animal poison control centre first
- Bring the pill vial, bait station or container to the veterinary surgeon so that it can be assessed for verification of the product name
- Call the original pharmacy to find out how many pills were prescribed and attempt to back-count how many were taken/ingested
- Seek immediate veterinary attention if the substance and quantity consumed are considered toxic

19.3 Owners often need to be encouraged to seek veterinary treatment. An experienced veterinary nurse or veterinary surgeon should speak with owners to make sure that patients receive appropriate treatment and advice.

Decontamination

Once the patient is stabilized, decontamination can be considered if appropriate. Human medicine has moved away from simple decontamination techniques, such as inducing emesis and administration of activated charcoal, due to the availability of more effective modalities, such as antidotes and techniques for extracorporeal toxin removal (e.g. plasmapheresis and haemodialysis). However, in veterinary medicine, pet owners' financial limitations often hinder the ability to treat patients in the same manner as human poisonings, and therefore the primary treatment for the poisoned patient should be decontamination and detoxification.

The goal of decontamination is to inhibit or minimize further toxicant absorption and to promote excretion or elimination of the toxicant from the body (Peterson, 2013). Decontamination can only be performed within a narrow window of time for most substances, therefore, it is important to obtain a thorough history and time since exposure. Although toxicant dependent, decontamination may significantly reduce absorption; however, contraindications for decontamination exist, and it is important to recognize that although the principles behind decontamination are sound, there are few randomized controlled studies in veterinary medicine that show improved outcome for any method of decontamination. Caution should be used prior to initiating decontamination, with careful consideration of questions such as:

- What is the route of exposure?
- Is there a significant risk of toxicosis based on a known dose–response relationship (exposure assessment and hazard risk)?
- Is the toxicant known and are there specific contraindications for decontamination in this patient?
- How long has it been since exposure?
- Did the owner (or referring veterinary surgeon if relevant) attempt decontamination prior to presentation?
- Is this patient suffering from respiratory or neurological dysfunction?
- Should other resources be consulted (e.g. animal poison control centre)?

Decontamination categories that prevent absorption or enhance elimination of the toxicant may include ocular, dermal, inhalation, gastrointestinal (GI), forced diuresis and surgical removal. While this chapter reviews the most common forms of decontamination in veterinary medicine, the reader is referred to a toxicology resource for additional information.

Dermal and ocular decontamination

Topical decontamination may be indicated for dermal and ocular exposure to a toxicant. The fur can be clipped if necessary, and then the skin washed with copious amounts of warm water with a mild detergent (e.g. washing up liquid). Multiple cycles of washing/rinsing are often recommended. Appropriate monitoring of thermoregulation is imperative after dermal decontamination to prevent secondary hypothermia post-bathing. 'Neutralizing' agents (e.g. acid for an alkaline toxicosis) should never be used, as they can result in more severe injury.

Gastrointestinal decontamination

GI decontamination is the most common type of decontamination performed in the small animal poisoned patient. Decontamination consists of both gastric evacuation (by emesis induction, gastric lavage, whole-bowel irrigation) and the administration of activated charcoal. Several contraindications exist, however, and the veterinary surgeon should be aware of when GI decontamination may be inappropriate or even hazardous.

Induction of emesis

Emesis induction is often initiated by an owner in the home with either 3% hydrogen peroxide or washing soda crystals. Syrup of ipecac is no longer recommended (Lee, 2011; Hojer, 2013; Peterson, 2013). Induction of emesis at home may not always be successful and may be associated with risk to the patient; wherever possible it is recommended that it is carried out under the supervision of a veterinary surgeon. Since gastric evacuation is time-dependent, animal poison control centres (e.g. Veterinary Poisons Information Service, Animal Poison Control Center) should be consulted promptly to identify if emesis induction is appropriate.

In dogs, apomorphine and hydrogen peroxide (3% only) are equally effective emetic agents (see Figure 19.4 for a summary of effective, safe emetic agents and their dosing). Side effects of apomorphine include sedation, bradycardia and protracted vomiting, while side effects of hydrogen peroxide include protracted vomiting, gastrointestinal ulceration (Niedzwecki *et al.*, 2016) and haemorrhagic gastritis (particularly in cats). For cats, alpha-agonists (e.g. xylazine,

Emetic agent	Where it works	Dose	Indicated for this species only
Hydrogen peroxide (3%)	Local gastric irritant	1–5 ml/kg orally up to two times; maximum of 50 ml/dog	Dogs
Apomorphine	CRTZ	0.03 mg/kg i.v. or 0.04 mg/kg i.m. is typically sufficient, although higher or repeated doses may be required. Crush tablet for subconjunctival administration (typically 6.25 mg tablets)	Dogs
Xylazine	Centrally acting alpha-agonist	0.44 mg/kg i.m. (reverse with yohimbine or atipamezole post-emesis)	Cats
Dexmedetomidine		7 µg/kg i.m. (reverse with yohimbine or atipamezole post-emesis if needed)	Cats

19.4 Emetic agents for use in dogs and cats. Every veterinary practice should keep these drugs in the pharmacy in case of a toxin exposure. Antiemetics are recommended to stop protracted vomiting. CRTZ = chemoreceptor trigger zone.

dexmedetomidine (see Thawley and Drobatz, 2015; Willey *et al*., 2005)) are the only emetics recommended; apomorphine is typically ineffective for cats. Side effects of alpha-agonists include sedation and bradycardia, which can be reversed with yohimbine or atipamezole.

Induction of emesis should be attempted when ingestion is recent (e.g. 1–2 hours) in asymptomatic patients (Lee, 2011). Delayed induction of emesis (up to 4–6 hours post-ingestion) is only recommended if the patient remains asymptomatic and if the toxicant is known to stay in the stomach for long periods of time (e.g. chocolate, grapes, large wads of chewing gum containing xylitol, massive ingestions, tablets that result in bezoar formation) (Lee, 2011).

Gastric lavage is considered a second form of gastric emptying for use when emesis is contraindicated and the toxicant is still thought to be present in the stomach. These situations are summarized in Figure 19.5. The clinical efficacy of gastric lavage is unknown in veterinary patients. In experimental studies in dogs, even when gastric lavage was performed within a short amount of time (15–20 minutes) after barium or sodium salicylate ingestion, recovered toxin was minimal (38% and 29%, respectively). After 60 minutes, the recovery of these toxicants is even less impressive (8.6–13%) (Kulig, 2004; Lee, 2011; Peterson, 2013).

Indications for gastric lavage

- Symptomatic patients predisposed to aspiration pneumonia due to decreased gag reflex (e.g. obtunded, comatose, tremoring, seizuring) that still require controlled decontamination (e.g. metaldehyde, organophosphates, carbamates) but in which induction of emesis is contraindicated
- Massive ingestions that may result in a foreign body obstruction (e.g. bone meal, blood meal, unbaked yeast bread dough)
- Massive ingestions that may result in a medical bezoar or concretion (e.g. large wads of chewing gum containing xylitol, iron capsules, aspirin, multi-vitamins, chocolate, cat litter)
- Drugs approaching the LD_{50}
- Drugs with a narrow margin of safety or those that result in severe clinical signs (e.g. calcium channel blockers, beta-blockers, cholecalciferol, organophosphates, baclofen, macrocyclic lactones, metaldehyde)

Contraindications for performing gastric lavage

- Risk of gastric perforation (e.g. patient with stomach ulceration or at risk of ulceration)
- Ingestion of a sharp, volatile, corrosive or caustic substance
- Patients at risk of cardiovascular collapse or otherwise poor anaesthetic candidates
- Failure to obtain and protect the airway
- Toxicants that result in severe aspiration pneumonitis (e.g. hydrocarbons, petroleum distillates)

19.5 Indications and contraindications for gastric lavage in small animal patients. Gastric lavage should be performed under general anaesthesia. An endotracheal tube should be properly placed and the cuff properly inflated. LD50 = dose at which mortality is 50%.

Gastric lavage can be labour intensive; however, despite all the above considerations, it is potentially life-saving. Patients should be anaesthetized and intubated, with the cuff of the endotracheal tube inflated to prevent secondary aspiration pneumonia. A step-by-step approach to performing gastric lavage is provided in Figure 19.6.

1. Prepare the following materials prior to sedation: intravenous catheter supplies; sedatives (pre-drawn and appropriately labelled); endotracheal tube; syringe to inflate endotracheal tube cuff; gauze (to secure endotracheal tube); anaesthetic or oxygen machine; appropriate monitoring devices; appropriately sized orogastric tube; roll of white tape or mouth gag; empty bucket; warm lavage water in a bucket; bilge or stomach pump or funnel; activated charcoal (pre-drawn in 60 ml syringes ready for administration, if indicated); and sedation reversal agents if necessary.
2. After placing the intravenous catheter, anaesthetize the patient and secure the airway. Connect to oxygen ± inhalant anaesthesia source. Place the patient in right lateral or sternal recumbency.
3. Administer a potent antiemetic (e.g. maropitant, ondansetron) to prevent secondary aspiration pneumonia upon extubation. Prepare an appropriately sized orogastric tube by pre-measuring it to the last rib; mark this line with white tape as this will be the maximum distance to insert the tube.
4. Lubricate the orogastric tube and gently pass the tube into the oropharynx, down the oesophagus, and into the stomach using gentle, twisting motions. Simultaneous inflation (e.g. blowing into the tube) will assist with passage of the tube into the stomach.
5. Confirm appropriate orogastric tube placement. This can be achieved by:
   - Palpating the neck for two tube-like structures (i.e. the trachea and the orogastric tube within the oesophagus)
   - Palpating the tube within the abdomen (on palpation of the exterior of the body wall)
   - Obtaining gastric contents or gas upon orogastric tube placement
   - Insufflating the orogastric tube while simultaneously auscultating for gurgling sounds within the stomach.
6. Once the tube is in the stomach, infuse tepid or warm water via the bilge/stomach pump or via gravity through the funnel. The volume of the stomach is approximately 90 ml/kg, therefore copious amounts of fluid can be used to lavage. Some sources recommend using 10 ml/kg per gavage, with 15–20 gavage cycles. Lower the end of the tube into an empty bucket, allowing the gastric contents and infused fluid to be recovered by gravity/siphon.
7. During the procedure, frequently palpate the stomach to prevent over-distension. Aggressive agitation of the stomach during lavage can enhance gastric lavage recovery. Multiple gavage cycles should be performed.
8. Gastric lavage fluid can be submitted for toxicological testing at a veterinary diagnostic laboratory if needed; the fluid should be examined for the presence of the toxicant prior to submission.
9. Once the stomach is emptied of gavage fluid, administer activated charcoal via the orogastric tube. The activated charcoal can be flushed in with a small amount of water or by insufflating the tube.
10. The orogastric tube must be 'kinked off' prior to removal in order to prevent fluid from being accidentally aspirated.
11. Recover the patient in sternal recumbency with the head elevated; extubate once a strong gag reflex is present.

19.6 How to perform gastric lavage.

Activated charcoal

The second step of decontamination is the administration of activated charcoal. Activated charcoal has a large surface area that binds toxicants (adsorbent) through inter- and intramolecular non-covalent bonds. Activated charcoal is available in various formulations (with and without an osmotic cathartic such as sorbitol). The dose of activated charcoal for single-dose treatment is 1–5 g/kg with a cathartic.

Activated charcoal should only be administered to the poisoned patient when warranted and medically appropriate. When a toxicant cannot be identified but there is a high suspicion of poisoning, it is reasonable to give a single dose of activated charcoal. However, it should not be given when the toxicant does not reliably bind to activated charcoal (e.g. heavy metals, xylitol, ethylene glycol, alcohol) or when it is contraindicated (e.g. salt toxicosis, corrosives, hydrocarbons) (Lee, 2011; Peterson, 2013). In addition, symptomatic patients who are at risk for aspiration pneumonia (e.g. decreased gag reflex) should not receive oral activated charcoal. Other contraindications for activated charcoal administration include patients requiring endoscopy (due to decreased visualization), when there is risk of a pharmacobezoar (functional ileus) or in the patient with mechanical ileus.

Administration of an osmotic cathartic in combination with activated charcoal is contraindicated in patients that are severely dehydrated or have underlying free water loss (e.g. renal disease, diabetes mellitus), due to the risk of hypernatraemia secondary to free water loss into the GI tract (Lee, 2011; Peterson, 2013). In the human medical literature, approximately 0.5% of people develop significant hypernatraemia (>155 mmol/l Na^+) after receiving multiple doses of activated charcoal (Dorrington *et al*., 2003).

Activated charcoal should be given as soon as possible after toxin ingestion to be most effective. In veterinary medicine, this is almost impossible due to travel time (to the clinic), lapsed time since ingestion, time to triage, and the amount of time it takes physically to deliver the activated charcoal (e.g. syringe feeding, orogastric tube). As a result, administration of activated charcoal is often delayed up to an hour or more. As time since ingestion is often unknown (e.g. owner coming home from work to find the pet poisoned), decontamination (including emesis and administration of activated charcoal) is often a relatively benign, albeit not always efficacious, course of action, provided the patient is not already symptomatic. In veterinary medicine, administration of activated charcoal with a cathartic as long as 6 hours after exposure may still be beneficial in certain types of toxicosis, particularly if the product is a delayed-release (e.g. extended- or sustained- release) toxicant, if it has a very long half-life (e.g. naproxen, 72 hours) or if it undergoes enterohepatic recirculation (see below). Figure 19.7 lists specific contraindications for activated charcoal.

Multiple doses of activated charcoal: The use of multiple doses of activated charcoal is warranted in the following situations (Lee, 2011):

- When the toxicant undergoes enterohepatic circulation
- Following ingestion of an extended-release drug
- For drugs that have a long half-life.

Historically, a loading dose of activated charcoal has been administered followed by repeated doses. It is unknown whether the frequency or the total dose is more important for decontamination. When administering multiple doses of activated charcoal, additional doses should *not* contain a cathartic (e.g. sorbitol), due to increased risk of free water loss into the GI tract and secondary hypernatraemia. The current recommended dose for multiple doses of activated charcoal is 1–2 g/kg of bodyweight *without a cathartic* orally q6h for approximately 24 hours.

Currently, there is no evidence in human or veterinary medicine that giving single or multiple doses of activated charcoal has an effect on clinical outcome (Chyka *et al*., 1995; Vale *et al*., 1999; Krenzelok and Vale, 2005). However, it is reasonable to treat with activated charcoal when there is a risk of toxicosis rather than withholding treatment, because the potential benefit may outweigh the risk of not giving activated charcoal.

Patient-related contraindications

- Central nervous system depression (decreased level of consciousness)
- Gastrointestinal disease (ileus/stasis, obstruction or perforation)
- Airway compromise or other condition predisposing to aspiration pneumonia (e.g. absent gag reflex, laryngeal paralysis, megaoesophagus, upper airway disease)
- Dehydration or hypovolaemia
- Electrolyte derangements (e.g. hypernatraemia) or hyperosmolar states (e.g. renal disease, diabetes mellitus, psychogenic polydipsia, diabetes insipidus)
- Imminent endoscopy or surgery

Toxin-related contraindications

- Ingestion of corrosive/caustic agents
- Toxicants that do not reliably bind to activated charcoal (e.g. ethylene glycol, xylitol, heavy metals)
- Ingestion of hydrocarbons or petroleum distillates
- Ingestion of salt or toxicants that can result in hypernatraemia (e.g. homemade play dough, sea water, table salt, paintballs)

19.7 Before administering activated charcoal the veterinary surgeon should determine whether there are any contraindications for this decontamination treatment.

Whole-bowel irrigation

The use of whole-bowel irrigation is rarely recommended for the poisoned veterinary patient. Typically, it is indicated following massive ingestions that require enhanced elimination from the GI tract (e.g. iron toxicosis). Polyethylene glycol solution can be administered via an orogastric or nasogastric tube in large volumes until the rectal effluent is clear. This technique has been used extensively in humans, especially those requiring lower GI endoscopy. Contraindications for whole-bowel irrigation include those patients at risk of aspiration or those with underlying ileus, perforation, cardiovascular instability, uncontrollable vomiting or GI haemorrhage (Thanacoody *et al*., 2015). For more information on whole-bowel irrigation, the reader is referred to toxicology textbooks.

Diagnostic toxicology

In the poisoned patient, it may be important to collect a variety of diagnostic samples depending on the suspected toxin, history and any clinical signs present. Appropriate diagnostic testing often includes several of the following: haematology, serum biochemistry panel, venous or arterial blood gas analysis, lactate, electrolytes, urinalysis, prothrombin time (PT), activated partial thromboplastin time (aPTT), packed cell volume (PCV), total solids (TS) and blood glucose.

Other samples may be useful for specific diagnostic toxicology, including whole blood (for rodenticide panels),

serum (for metal analysis) and urine (for illicit, recreational drugs). Post-mortem analysis is not routine in veterinary medicine; however, it is available for clients interested in confirmation of a diagnosis (e.g. suspected malicious, intentional poisoning). Ingesta and frozen biopsy samples (including liver, kidney, brain and fat) can be submitted to rule out certain toxins (e.g. rodenticides, ethylene glycol, heavy metals, strychnine). It is advised to consult with a veterinary diagnostic laboratory prior to collection of samples to ensure appropriate samples and collection techniques. In the UK a toxicological diagnostic service is provided by CTDS (www.ctdslab.co.uk).

Symptomatic treatment and supportive care

Monitoring

In the poisoned patient, appropriate monitoring is imperative. Assessing the patient for response to treatment is useful for determining prognosis, length of treatment or the need for alternative therapies. The poisoned patient should be monitored for respiratory distress (e.g. increased respiratory rate or effort, hypoventilation, hypoxaemia, cyanosis), cardiovascular stability (e.g. heart rate and rhythm, pulse pressure quality, capillary refill time (CRT), mucous membrane colour) and neurological function (e.g. mentation, seizure activity, tremors, brainstem reflexes, motor function). The patient should also be monitored for fluid losses and imbalance (e.g. urine output, GI losses, ptyalism, panting, third-spacing and peripheral oedema).

In the critically ill poisoned patient, intensive monitoring may be necessary (e.g. blood pressure, pulse oximetry, blood gas analysis, electrocardiography, end-tidal carbon dioxide, body temperature, central venous pressure and urine output) (Lee, 2011). As clinical signs of hypertension, hypotension, tachycardia, bradycardia, arrhythmias, tremors and seizures are often seen in the poisoned patient, monitoring often necessitates frequent or continuous blood pressure and electrocardiogram monitoring. Referral to a 24-hour facility may be required to provide continued supportive care, especially if the clinical course of the toxicosis is worsening or is expected to exceed 12 hours.

Supportive care

Appropriate symptomatic and supportive care is paramount for effective treatment once the poisoned patient has been decontaminated. There are several broad categories of treatment that should be considered, including:

- Fluid therapy
- GI support
- Central nervous system (CNS) support
- Sedation and reversal agents
- Hepatoprotectants.

Fluid therapy

Fluid therapy is the cornerstone of emergency treatment of the poisoned patient. The rationale to administer fluid therapy includes the following:

- Improve cardiac output and assure adequate cellular oxygen delivery
- Correct or prevent dehydration and hypovolaemia
- Aid in renal elimination of toxicants through diuresis
- Maintain renal blood flow (particularly with nephrotoxicants)
- Correct metabolic derangements (e.g. metabolic acidosis) and electrolyte imbalances (e.g. hypokalaemia, hypercalcaemia)
- Treat hypotension (e.g. beta-blockers, calcium channel blockers)
- Restore oxygen-carrying capacity with packed red blood cells or whole blood following blood loss (e.g. rodenticide coagulopathy, bleeding GI ulcer).

Poisoned patients typically benefit from intravenous isotonic, balanced crystalloids. Diuresis is achieved in a healthy patient with fluid rates of 4–8 ml/kg/h. Paediatric patients have an inherently higher maintenance fluid requirement (80–180 ml/kg/day) depending on age, and may require more aggressive fluid rates. Fluid therapy should be administered judiciously to patients with underlying cardiopulmonary disease, to prevent secondary pulmonary oedema. Though rare, tricyclic antidepressants and exposure to zinc phosphide rodenticides can predispose a patient to cardiogenic pulmonary oedema and acute lung injury, and fluid therapy should be titrated appropriately.

A patient's hydration and volume status should be evaluated frequently while hospitalized. Tachycardia, poor pulse quality, pale mucous membranes, prolonged CRT, weight gain or loss, haemoconcentration (based on PCV/TS), pre-renal azotaemia and hypersthenuria (urine specific gravity: cats >1.040; dogs >1.025) are all gross indicators of poor fluid balance. The clinician should act on these data in order to maintain perfusion and hydration. Prolonged hypoperfusion may lead to worsening clinical signs, development of comorbidities (e.g. acute kidney injury (AKI), ischaemic brain injury, metabolic acidosis) and risk of death. Ideally, previously normal, healthy patients that have been exposed to a toxin should be appropriately haemodiluted to a PCV/TS of 35% and 50 g/l while on intravenous fluids; however, the end points may be different in patients with concurrent haemorrhage or other underlying disease.

Gastrointestinal support

Ulcer prophylaxis and antiemetics are often indicated for the poisoned patient. Antiemetics may be indicated if vomiting is a presenting complaint or if there is prolonged vomiting following induction of emesis. Antiemetics and prokinetic drugs often benefit the nauseous patient (as evidenced by discomfort on palpation of the stomach, lip-licking, ptyalism, hypo- or anorexia, or gastric ileus or distension). Prophylactic antiemetics should be used to prevent vomiting following the administration of activated charcoal or other oral medications. Patients that have ingested certain medications associated with increased risk of GI ulceration (e.g. corrosives, non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids) should be treated, even in the absence of clinical signs, with antacids (e.g. H2 blockers, proton pump inhibitors) and anti-ulcer drugs (e.g. sucralfate). Dosages can be found in Figure 19.8.

Central nervous system support

In small animals, clinical signs of CNS stimulation (e.g. agitation, tremors, seizures) and inhibition (e.g. sedation, coma) are frequently caused by toxicants. Toxicants that result in significant CNS signs include amphetamines, selective serotonin reuptake inhibitors (SSRIs), sleep aids

Drug	Dose	Indication
Dolasetron	0.6–1 mg/kg orally, s.c., i.v. q24h	Antiemetic
Maropitant	1 mg/kg s.c., i.v. q24h	Antiemetic
Ondansetron	0.1–1 mg/kg orally, i.v. q8–12h	Antiemetic
Metoclopramide	0.1–0.5 mg/kg orally, s.c., i.m. q6–8h or 1–2 mg/kg/day as a CRI	Antiemetic; prokinetic
Cimetidine	5–10 mg/kg orally q6–8h	H2 blocker
Famotidine	0.5–1 mg/kg orally, s.c., i.v. q12–24h	H2 blocker
Ranitidine	0.5–2 mg/kg orally, s.c., i.m., i.v. q8–12h	H2 blocker
Omeprazole	1 mg/kg orally q24h	Proton pump inhibitor
Pantoprazole	1 mg/kg i.v. q24h	Proton pump inhibitor
Sucralfate	0.1–1 g orally q8h depending on size of the patient	Anti-ulcer

19.8 Controlling, preventing and treating gastrointestinal signs is an important part of symptomatic and supportive care. Antiemetics should be given to control nausea and vomiting. Antacids and sucralfate are useful in the treatment and prevention of ulcers. CRI = constant rate infusion.

(e.g. zolpidem), methylxanthines (e.g. theobromine, caffeine), tremorgenic mycotoxins, aflatoxins, mouldy foods, pyrethrins/pyrethroids (in cats), metaldehyde and strychnine. The use of sedatives, anxiolytics, muscle relaxants and anticonvulsants may be necessary; see 'Sedatives and reversal agents' for more information on the use of anxiolytics. In tremoring patients, the use of centrally acting muscle relaxants (e.g. methocarbamol 55–110 mg/kg i.v. q6–8h to effect) is ideal. If the intravenous form of methocarbamol is not available, oral or rectal dosing can be used. For actively seizuring patients, anticonvulsants or general anaesthetics (e.g. benzodiazepines, phenobarbital, levetiracetam, propofol) should be administered intravenously. Doses of specific muscle relaxants and anticonvulsant drugs can be found in Figure 19.9.

Sedatives and reversal agents

Stimulation/excitatory signs such as anxiety are also frequent clinical findings in poisoned small animal patients. Common toxicants resulting in anxiety (seen as tachycardia, trembling, mydriatic pupils, apprehension, hypertension, aggression) include phenylpropanolamine, methylxanthines, albuterol, SSRIs, amphetamines and sleep aids. Treatment should include the use of anxiolytic drugs such as phenothiazines (e.g. acepromazine, chlorpromazine). In 50% of dogs clinically affected by sleep aid toxicosis, a paradoxical CNS stimulation may be seen. If observed, benzodiazepines are contraindicated; phenothiazines should be used instead.

Some toxicants have a reversal agent available. With opioid or baclofen toxicosis, the opioid reversal agent, naloxone, may be beneficial. In benzodiazepine toxicosis (or non-benzodiazepine sleep aids), the use of flumazenil can be considered in severely affected patients. With imidazoline decongestants (commonly found in nasal sprays and eye drops), alpha-2 adrenergic antagonists (e.g. yohimbine, atipamezole) are beneficial to counter the alpha-agonist activity of these sympathomimetic compounds. With reversal agents, frequent redosing is often necessary.

Hepatoprotectants

S-Adenosylmethionine (SAMe), *N*-acetylcysteine (NAC) and silybin (milk thistle) are generally recommended for animals exposed to hepatotoxicants. These hepatoprotectants are benign and should be considered for specific toxicants such as paracetamol/acetaminophen, xylitol, sago (*Cycad*) palms, *Amanita* mushrooms, blue-green algae, alpha-lipoic acid, aflatoxins and, possibly, NSAID hepatotoxicity. Both SAMe and NAC act as a source of glutathione and have antioxidant properties; SAMe also exhibits anti-apoptotic properties by modulating cytokines and stabilizing cell membranes. NAC has been shown to be anti-inflammatory and to improve microcirculation in the liver, allowing for improved oxygen delivery. Silybin (silymarin) is anti-fibrotic and anti-inflammatory, and also scavenges reactive oxygen species (Vogel *et al*., 1984; Webster and Cooper, 2009). Doses for hepatoprotectants can be found in Figure 19.10.

Drug	Dose	Indication
Levetiracetam	20 mg/kg orally, i.v. q8h; 30 mg/kg orally q12h using extended-release formulation; 30–60 mg/kg i.v. bolus for status epilepticus	Anticonvulsant
Phenobarbital	4–24 mg/kg i.v. loading dose; can be given as one dose or divided into 3–4 doses q2–4h; additional doses may be necessary	Anticonvulsant
Diazepam	0.5–1.0 mg/kg i.v. as needed to effect, followed by a CRI if indicated; 0.5 mg/kg can be given intranasally if no i.v. access (dogs)	Anticonvulsant; sedative
Midazolam	0.1–0.3 mg/kg i.m., i.v. as needed to effect, followed by a CRI if indicated; 0.2–0.5 mg/kg can be given intranasally if no i.v. access	Anticonvulsant; sedative
Propofol	1–6 mg/kg slow i.v. as needed to effect, followed by a CRI at 0.1–0.6 mg/kg/min as needed	Anticonvulsant; sedative
Acepromazine	0.005–0.1 mg/kg i.m., i.v., s.c. as needed to effect. In general, no more than 3 mg/dog total dose is recommended	Sedative
Butorphanol	0.2–0.8 mg/kg s.c., i.m., i.v. as needed to effect	Sedative
Chlorpromazine	Dogs: 0.1–0.5 mg/kg i.v., i.m., s.c. as needed to effect	Sedative
Inhalant agents (e.g. sevoflurane, isoflurane)	Via mask or endotracheal tube to effect	General anaesthetic to control seizures
Methocarbamol	55–110 mg/kg q6–8h as needed to effect; recommended total daily dose is 330 mg/kg but this can be exceeded, if necessary, with careful monitoring; CRI starting at 10 mg/kg/h titrated to effect	For the treatment of tremors; as a muscle relaxant
Naloxone	0.01–0.02 mg/kg i.v., s.c., i.m.	Opioid reversal

19.9 Doses for sedatives, reversal agents, muscle relaxants and anticonvulsant drugs. CRI = constant rate infusion.

Agent	Mechanism of action	Dose	Side effects
N-Acetylcysteine (NAC)	Increases glutathione; anti-inflammatory; improves microcirculation; improves oxygen delivery	140 mg/kg initially then 70 mg/kg i.v., orally q6h	Vomiting; thrombophlebitis; oral ulcers (if not appropriately diluted)
S-Adenosylmethionine (SAMe)	Increases glutathione; improves membrane stability; cytokine modulation; anti-apoptotic	18 mg/kg orally q24h on an empty stomach	None
Silybin/silymarin (milk thistle)	Reactive oxygen species scavenger; anti-inflammatory; anti-fibrotic; increases protein synthesis; choleretic	20–50 mg/kg orally q24h	Inhibits activity of drug-metabolizing enzymes
Ursodeoxycholic acid	Replaces hepatotoxic bile acids; choleretic; anti-apoptotic; immunomodulatory; stabilizes mitochondria	10–15 mg/kg orally q24h with food	Vomiting (rare)
Vitamin E	Antioxidant; anti-inflammatory	10–15 IU/kg orally q24h	None

19.10 Doses for hepatoprotective and cytoprotective agents. (Adapted from Webster and Cooper, 2009)

Antidotes

Antidotes are therapeutic agents that act specifically either to neutralize the toxin or antagonize the toxin's harmful consequences. A metal chelator is an example of a neutralizing antidote; NAC given in paracetamol toxicosis is an example of an antidote that helps to restore normal function. If an antidote is available, therapy should be initiated promptly once the patient has been stabilized. Unfortunately, antidotal therapy is limited in the small animal poisoned patient, due to both availability and cost, but the majority of poisoned patients respond to symptomatic supportive care. Limited antidotal therapy is reviewed in the discussion below, on specific toxicants. Intravenous lipid emulsion (ILE) may be used as a novel fat-soluble 'antidote' and is discussed below.

Intravenous lipid emulsion

ILE, also called intravenous fat emulsion, was originally used as part of total parenteral nutrition (TPN), partial parenteral nutrition (PPN) and as a vehicle for drug delivery (e.g. propofol); increasingly, it is also being used as a potential antidote for lipophilic drug toxicosis. Current theories about the mechanism of action of ILE in the poisoned patient include the following (Jamaty *et al*., 2010; Fernandez *et al*., 2011):

- Acting as a 'lipid sink' by sequestration of lipophilic compounds into the newly created intravascular lipid compartment (a lipid or pharmacological sink). With this lipid sink hypothesis, compartmentalization of the drug into the lipid phase results in lower free drug concentrations available to tissues
- Providing myocytes with an energy substrate (free fatty acids), thereby augmenting cardiac performance
- Restoring myocardial function by increasing intracellular calcium concentration through the direct activation of voltage-gated calcium channels in the myocardium
- Increasing the overall fatty acid pool, which overcomes inhibition of mitochondrial fatty acid metabolism (e.g. bupivacaine toxicosis).

Currently, the most supported hypotheses are that ILE improves cardiac performance and provides a lipid sink effect in the vascular compartment.

In veterinary medicine, the use of ILE has been advocated for severe clinical signs seen with toxicoses such as macrocyclic lactones (e.g. moxidectin, ivermectin) (Clarke *et al*., 2011), local anaesthetics (e.g. lidocaine), lipophilic gamma-aminobutyric acid (GABA) receptor agonists (e.g. baclofen) (Bates *et al*., 2013), calcium channel blockers (e.g. diltiazem), pyrethrins or pyrethroids (in cats), marijuana and NSAIDs (e.g. naproxen, ibuprofen).

A review by Fernandez *et al*. (2011) discussed recommendations on the use of ILE. In this review, dosage recommendations in veterinary medicine were based on extrapolation from human dosing and the dose used for TPN and PPN administration in veterinary medicine; off-label administration of an initial 20% ILE bolus in the range 1.5–4 ml/kg (between 0.3 and 0.8 g/kg i.v. over 1 minute), followed by a CRI of 0.25 ml/kg/min (0.05 g/kg/min) i.v. for 30–60 minutes, is a generally conservative start. In patients that are unresponsive after this dosing, the authors recommend intermittent boluses of 1.5 ml/kg q4–6h for 24 hours, with anecdotal success. Alternatively, follow-up CRI doses of 0.5 ml/kg/h (0.1 g/kg/h) can be continued until clinical signs improve (not to exceed 24 hours) or until serum is lipaemic. However, it should be borne in mind that there have been no safety studies evaluating the use of ILE in the clinically poisoned veterinary patient, and careful monitoring and risk assessment is imperative.

The ASPCA Animal Poison Control Center (Urbana, IL, USA) has experienced anecdotal success with the use of ILE for certain additional medications with a narrow margin of safety (e.g. baclofen, cholecalciferol, calcium channel blockers, beta-blockers). However, there are reports – in both human and veterinary medicine – where ILE has not been beneficial. In general, the use of ILE should be limited to life-threatening ingestions, severely symptomatic patients and those that fail to respond to traditional therapy. It should be kept in mind that rare adverse effects of this extra-label treatment include fat embolism, fat overload syndrome, pancreatitis, worsening of acute respiratory distress syndrome, corneal clouding due to lipid deposits or even coagulopathy. More importantly, in human medicine the use of ILE is generally reserved until late-stage or late treatment (e.g. once cardiopulmonary arrest has occurred), due to the risk of drug interaction (e.g. cardiopulmonary resuscitation drug therapy, anticonvulsants, muscle relaxants, sedatives) with ILE.

The administration of ILE for the treatment of lipophilic drug toxicosis in veterinary medicine is still in its infancy and the potential is currently unknown. Judicious use of this new potential antidote should be considered based on the lipophilic nature of the toxicant. Readers are directed to the most recent resources on ILE for further information.

Selected toxicants

Ethylene glycol

Description and exposure

Ethylene glycol is an odourless compound commonly found in high concentrations in radiator fluid, antifreeze, de-icing solutions and some industrial solvents. It is also found in low concentrations in substances such as paints, ink-jet printer and caulking material (e.g. sealants/fillers used in household maintenance), but these rarely result in toxicosis.

Mechanism of action

Ethylene glycol itself is not poisonous; rather, it is the metabolites of ethylene glycol that result in severe toxicosis. Hence, the goals of antidotal therapy for ethylene glycol toxicosis are to prevent the metabolism of ethylene glycol to these dangerous metabolites. Metabolism occurs primarily in the liver, where alcohol dehydrogenase converts ethylene glycol to glycoaldehyde and organic acids. Glycoaldehyde is ultimately metabolized to glyoxylate or glyoxylic acid. Glyoxylate when combined with calcium will form calcium oxalate crystals, resulting in nephrosis and secondary AKI.

Clinical presentation

CNS signs (e.g. ataxia, 'drunkenness', depression), profound polyuria/polydipsia and GI signs (e.g. hypersalivation, vomiting) may be seen as soon as 30 minutes after ingestion. CNS depression typically resolves in 12 hours in dogs. Signs of AKI (e.g. GI signs, ptyalism, uraemic halitosis, oral ulcerations, depression, anorexia, abdominal pain, oliguria, anuria) typically do not develop until 24–72 hours later. Once azotaemia has developed, the prognosis is grave, despite treatment.

Diagnostics

Veterinary-specific ethylene glycol tests can be used to help diagnose ethylene glycol toxicosis, although numerous false-positive results can be seen with propylene glycol (found in diazepam, methocarbamol and other injectable drugs), activated charcoal containing sorbitol, isopropyl alcohol and ethanol. Ideally, rapid quantitative measurement of ethylene glycol blood levels is the most accurate way of diagnosing ethylene glycol toxicosis. Other clinicopathological changes seen with ethylene glycol toxicosis include the presence of a metabolic acidosis (identified by a high anion gap and low bicarbonate) with normochloraemia; this can develop quite rapidly and can be severe. Ionized hypocalcaemia and hyperglycaemia are also very common, occurring in >50% of dogs and cats. Calcium oxalate crystalluria can be seen in the urine 3–8 hours post-exposure (Thrall *et al*., 1984). Likewise, an osmolar gap can be calculated and compared with the measured osmolar gap. The presence of a high osmolar gap is consistent with ethylene glycol toxicosis, but can also be consistent with lactic acidosis or uraemia. Finally, hyperphosphataemia and azotaemia will be appreciated as AKI develops.

Treatment

Ethylene glycol is rapidly absorbed from the GI tract. Performing GI decontamination more than 1 hour after exposure is not indicated. Furthermore, activated charcoal does not reliably bind to ethylene glycol, and is not typically warranted. Therapy should be targeted at decreasing metabolism to harmful metabolites with antidotal therapy in the form of either ethanol or fomepizole/4-methylpyrazole (4-MP); both have a stronger affinity for alcohol dehydrogenase than ethylene glycol. Antidotal therapy must be initiated within 3 hours in cats, and within 8–12 hours in dogs for the best outcome (see Figure 19.11 for doses). In cats, antidotal treatment initiated later than 3 hours post-exposure is ineffective, being associated with almost 100% fatality (Connally *et al*., 2010). Side effects of antidotal therapy can be seen, but are typically mild. Ethanol is associated with CNS depression and may further contribute to metabolic acidosis (through conversion of pyruvate to lactate) and hypoglycaemia; these side effects are generally not seen with 4-MP, which is generally considered safer. However, 4-MP is expensive and is not always available. The use of haemodialysis, if available, can be considered to remove ethylene glycol (and its harmful metabolites) prior to the onset of signs or to treat AKI.

Prognosis

Patients treated within 3 hours (cats) or within 8–12 hours (dogs) with 4-MP or ethanol have a fair prognosis. The presence of azotaemia or progression to anuric AKI represents a grave prognosis.

Antidote	Dose	Indications
Ascorbic acid (vitamin C)	30 mg/kg orally, s.c., i.v. q6h	Antioxidant
Atropine	0.02–0.2 mg/kg i.v., s.c., i.m. as needed; if there is a physiological response to a 0.02 mg/kg test dose (e.g. increased heart rate), look for another cause of the clinical signs; give ¼ of the dose i.v., remainder i.m. or s.c. to control signs up to every hour	Antimuscarinic antidote for organophosphate toxicosis Note: A much higher dose is required for organophosphate toxicosis compared with other indications
Cyproheptadine	Dogs: 1.1 mg/kg orally q4–6h or rectally as needed Cats: 2–4 mg (total dose) orally q4–6h or rectally as needed	Serotonin antagonist for use with toxicants causing serotonin syndrome (e.g. SSRIs, TCAs, amphetamines)
Ethanol 7% (70 mg/ml)	Load with 8.6 ml/kg (600 mg/kg) slow i.v. once, followed by 1.43 ml/kg/h (100 mg/kg/h) i.v. as a CRI for 24–36 hours or until the ethylene glycol test is negative	Competitive inhibitor of alcohol dehydrogenase used for ethylene glycol poisoning (when fomepizole is not available)
Fomepizole/4-methylpyrazole (4-MP)	Dogs: 20 mg/kg i.v. initially; at 12 h give 15 mg/kg i.v.; at 24 h give 15 mg/kg i.v.; at 36 h give 5 mg/kg i.v. Cats: 125 mg/kg i.v.; at 12, 24, 36 h give 31.25 mg/kg i.v.	Synthetic alcohol dehydrogenase inhibitor for ethylene glycol poisoning
Pralidoxime chloride (2-PAM)	20 mg/kg slow i.v. (over 5 min) i.m., s.c. q6–12h	Cholinesterase reactivator for the treatment of organophosphate toxicosis Note: Usually administered concurrently with atropine

19.11 Miscellaneous drugs and antidotes used for the poisoned patient. SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant.

Anticoagulant rodenticides

Description and exposure

Anticoagulant rodenticide (ACR) exposure occurs by ingestion of rodenticide bait products. Cats are more resistant to ACR compared with dogs. Relay toxicosis (secondary to ingestion of poisoned mice) is rare in dogs and cats.

Mechanism of action

ACRs act by blocking the conversion of inactive, oxidized vitamin K to its active, reduced form (vitamin K hydroquinone). When active vitamin K is depleted, the liver is unable to activate coagulation factors II, VII, IX and X, resulting in a life-threatening coagulopathy. Cavitary bleeding, as well as bleeding into the pulmonary parenchyma, pericardium, GI tract, skin and from the nasal mucosa, are some sequelae of coagulopathy.

Clinical presentation

The time from exposure to the development of clinical signs is typically 3–5 days post-ingestion; thus, patients acutely exposed to rodenticide (<24–36 hours) may present without clinical signs or evidence of coagulopathy. Those presenting with clinical signs typically show evidence of coagulopathy and haemorrhagic shock. Dyspnoea, haemoptysis, tachycardia, pallor, poor pulse quality, tachypnoea and altered mentation are commonly seen. Melena, epistaxis, petechiae, bleeding from the gums and ecchymoses are less common.

Diagnostics

A PT should be measured to assess the degree of coagulopathy. Factor VII has the shortest half-life (6.2 hours) of the vitamin K-dependent coagulation factors and depletion is seen at approximately 36–48 hours. Evaluation of the extrinsic coagulation pathway through PT evaluation will confirm a toxic dose of ACR. A prolonged PT (usually prolonged out of range) is a typical finding with clinical evidence of bleeding. Routine bloodwork (haematology and serum chemistry) can be performed to assess for anaemia and to rule out other causes of coagulopathy (e.g. thrombocytopenia). Whole blood and gastric contents can be submitted for confirmation of the presence of ACR, if indicated; however, results are often delayed for several days, and treatment should not be withheld in a clinically symptomatic patient. Radiography and ultrasonography (especially focused assessment with sonography for trauma (FAST) scans) should be considered to look for evidence of cavitary bleeding (e.g. pleural effusion, pericardial effusion, abdominal effusion).

Treatment

Patients recently exposed to ACR should be decontaminated, typically with induction of emesis and administration of one dose of activated charcoal. Following decontamination, there are two main strategies for treatment and follow-up. The first is for the concerned pet owner who elects to treat regardless of whether the patient is coagulopathic or not. With this method, treatment with oral vitamin K1 (3–5 mg/kg divided q12h for 30 days) can be started immediately. The second strategy is a more hands-off approach that requires decontamination and then monitoring of PT (without any initial vitamin K1 therapy). In this second technique, the patient should be appropriately decontaminated; no vitamin K1 is started, rather, a PT is assessed approximately 36–48 hours post-exposure. Depending on what the PT results are, vitamin K1 therapy can be initiated if necessary (3–5 mg/kg divided q12h for 30 days). For both of these strategies, a recheck PT should be performed 48 hours after the last dose of oral vitamin K1 (approximately day 32); if prolonged, an additional 2 weeks of therapy is warranted. It should be noted that an initial one-time injection of vitamin K1 should be avoided unless followed by 30 days of treatment with vitamin K1, as this will alter results of a PT 48 hours post-exposure. In the acutely poisoned ACR patient, fluid therapy, hospitalization and supportive care in a hospital environment is typically not necessary.

If the patient presents clinically bleeding from coagulopathy, treatment with fresh frozen plasma (FFP) or frozen plasma (FP) is warranted to replace clotting factors. Vitamin K1 alone is not curative, as normalization of PT takes approximately 12 hours following initiation of therapy, therefore acute bleeding secondary to coagulopathy requires factor replacement if signs of bleeding are present. Supportive care in the form of oxygen therapy, crystalloid fluids, plasma transfusions and even whole blood transfusions may be necessary. Concurrent treatment with vitamin K1 for 30 days should be initiated. When administering vitamin K1, oral administration is preferable to parenteral administration due to rapid absorption from the GI tract.

Prognosis

Early decontamination and treatment is associated with an excellent prognosis. Clinically bleeding patients also have an excellent prognosis if treatment is immediate and appropriate.

Metaldehyde

Description and exposure

Dogs are most commonly exposed to metaldehyde in slug and snail baits. It is also found as a solid fuel for some camp stoves.

Mechanism of action

Metaldehyde is suspected of increasing excitatory neurotransmitters or decreasing inhibitory neurotransmitters, thereby reducing the seizure threshold.

Clinical presentation

Clinical signs of metaldehyde toxicosis are generally referred to as ‘shake and bake’ and include agitation, tremors, seizures and severe hyperthermia. Disseminated intravascular coagulation (DIC) and organ failure can develop secondary to severe hyperthermia. Hepatotoxicity has been reported, although this is rare (Dolder, 2003).

Diagnostics

Abdominal radiography may be useful as pellets are often radiopaque. The presence of suspicious material in the stomach on radiographs warrants appropriate gastric decontamination via gastric lavage in a symptomatic patient.

Treatment

Treatment should include GI decontamination (e.g. gastric lavage and a single dose of activated charcoal administered via the orogastric tube at the end of lavage). Tepid water enemas can also be administered to facilitate lower

GI emptying. Intravenous fluid therapy, anticonvulsants (e.g. phenobarbital, benzodiazepines), muscle relaxants (e.g. methocarbamol, anxiolytics) and monitoring of hepatic function are recommended until clinical signs resolve. In severe cases with intractable seizures, general anaesthesia may be required, sometimes for >24 hours. If significant hyperthermia occurs, coagulation should be monitored and DIC treated as needed. Signs should resolve 24–72 hours after exposure.

Prognosis

Good to excellent with several days of supportive and symptomatic care.

Non-steroidal anti-inflammatory drugs

Description and exposure

NSAIDs are common human (e.g. ibuprofen, naproxen, aspirin) and veterinary (e.g. carprofen, meloxicam, firocoxib) analgesics. Exposure may be accidental (especially with palatable chewable forms of the drugs) or by owner-induced overdose.

Mechanism of action

NSAIDs are competitive inhibitors of cyclo-oxygenase (COX) enzymes, resulting in decreased production of constitutive prostaglandins that are vital for homeostasis and maintenance of renal blood flow and gastric mucosal integrity. As such, toxicosis can result in GI upset, including ulceration, and AKI. In dogs, ibuprofen doses >50 mg/kg can result in gastric ulceration, doses >175–200 mg/kg can result in AKI, and doses >400 mg/kg are associated with seizures and death (Villar and Buck, 1998). For veterinary NSAIDs in dogs, the general guideline is that >5 times the therapeutic dose may result in GI signs, while >10 times the therapeutic dose may result in AKI. Cats are considered to be at least twice as sensitive to NSAIDs as dogs.

Clinical presentation

NSAID toxicosis may include clinical signs of anorexia, vomiting, haematemesis, diarrhoea, melena, pallor, acute abdomen, uraemic halitosis, polyuria, polydipsia, anuria and colic.

Diagnostics

A minimum database of haematology, serum biochemistry and urinalysis (including urine specific gravity prior to fluid therapy) is recommended if a patient has ingested a dose that can result in nephrotoxicity. Monitoring for clinicopathological evidence of GI ulceration (e.g. hypoproteinaemia, anaemia, elevated blood urea nitrogen), perforation (e.g. initial hyperglycaemia, hypoglycaemia, presence of band neutrophils, cytological evidence of septic peritoneal effusion) or AKI (e.g. hyperphosphataemia, azotaemia, isosthenuria prior to fluid administration) should occur.

Treatment

Depending on the toxic dose ingested, aggressive treatment of NSAID exposure is recommended. Induction of emesis and administration of activated charcoal are often recommended. Multiple doses of activated charcoal should be considered if the NSAID undergoes enterohepatic circulation (e.g. carprofen, ibuprofen) or has a long half-life (e.g. naproxen, 72 hours). GI medications should include antiemetics and ulcer prophylaxis with antacids (e.g. H2 blockers, proton pump inhibitors) and sucralfate. Synthetic prostaglandins (e.g. misoprostol) can be considered to increase gastric mucus production, mucosal blood flow and healing; however, misoprostol has unknown efficacy in the prevention or treatment of gastric ulcers. Depending on the dose ingested, aggressive intravenous fluids are recommended to maintain renal perfusion and to aid in vasodilation of renal vessels. Transfusion therapy may be necessary if significant bleeding secondary to gastric ulceration occurs.

Prognosis

With aggressive treatment, the prognosis for NSAID toxicosis is excellent if treated early. However, once azotaemia, oliguria or anuria has developed, the prognosis is poor to guarded.

Paracetamol

Description and exposure

Paracetamol (*N*-acetyl-*p*-aminophenol), otherwise known as acetaminophen, is an OTC analgesic and antipyretic for humans. Most animals are exposed through accidental ingestion or uninformed owner administration.

Mechanism of action

Normally, paracetamol is metabolized to a non-toxic conjugate. Toxicosis occurs when the glucuronidation and sulphation pathways are saturated, in which case a toxic metabolite, *N*-acetyl-*p*-benzoquinoneimine (NAPQI), is generated via the cytochrome p450 pathway. NAPQI can be conjugated with glutathione and is detoxified, but NAPQI accumulation results in oxidative injury, methaemoglobinaemia (metHb) and hepatic injury. Cats have a decreased capacity for glucuronidation, are more susceptible to toxicosis, and have a much lower toxic dose (10 mg/kg) compared with dogs (100–150 mg/kg).

Clinical presentation

Cats may present with severe, acute clinical signs within an hour of exposure. Swelling of the face and paws, GI signs (e.g. anorexia, hypersalivation, vomiting), respiratory distress, brown mucous membranes, cyanosis, tachypnoea and dyspnoea may be seen. In dogs, clinical signs may be similar, although hepatic failure is more likely to be seen than development of metHb. Signs of hepatic failure may take 24–48 hours to manifest, and include malaise, anorexia, vomiting, hypersalivation, elevated liver enzymes, icterus, hepatic encephalopathy and death. Rarely, keratoconjunctivitis sicca has been reported in dogs secondary to paracetamol exposure, even at sub-toxic levels.

Diagnostics

Haematology, serum biochemistry and a blood smear should be performed when toxic doses have been ingested. A haematocrit tube should be evaluated for the presence of chocolate-brown colour (evidence of metHb). While not commonly available, a multi-wavelength co-oximeter can be used to measure metHb. Human hospitals may be able to measure quantitative paracetamol levels, which may help establish prognosis or determine if treatment is necessary.

Treatment

As paracetamol is rapidly absorbed from the GI tract (with peak plasma levels being achieved as little as 20 minutes after ingestion), emesis induction is not warranted. Rather, immediate use of activated charcoal with a cathartic is preferred. Stabilization is warranted in severely affected paracetamol toxicosis cases, and includes oxygen therapy, intravenous fluid therapy, antiemetics, blood products (to provide functional haemoglobin) and supportive care. Antioxidants (e.g. vitamin C) and hepatoprotectants or glutathione precursors (SAMe and NAC) reduce and limit the production of NAPQI, the harmful metabolite, and should be instituted immediately. The use of cimetidine (to inhibit cytochrome p450 metabolism) is no longer recommended for paracetamol toxicosis, as it has not been found to be beneficial. In cases with severe metHb, the use of methylene blue can be considered; its use should be limited to dogs, due to the risk of Heinz body anaemia when used in cats. Treatment for liver injury or failure may be indicated (e.g. vitamin K1, FFP). In dogs, if liver values are within normal limits after 48 hours of NAC treatment, the patient can be successfully discharged. The veterinary surgeon should refer to an appropriate reference for more information to treat hepatic failure (Berent and Rondeau, 2009).

Prognosis

Poor in patients with severe hepatoxicity.

Pyrethroids and pyrethrins

Description and exposure

Pyrethrins are an insecticide naturally derived from *Chrysanthemum* spp., a common flower. Pyrethroids are synthetic derivatives and analogues that are commonly used as low-concentration products (<1%) in household insecticides, sprays, shampoos and pet shampoos to high concentrations in topical spot-on flea and tick medications, and pet shampoos. Low concentration products are rarely toxic, even to cats. However, a more common source of toxicosis is the inappropriate application of a high-concentration (40–60%) pyrethrin canine product on a cat.

Mechanism of action

Pyrethrins and pyrethroids act by slowing the opening and closing of sodium channels, resulting in hyperexcitability of the cells. Cats are more at risk of developing toxicosis due to their inherent deficiency in glucuronidation; >5% pyrethrin concentrations can result in systemic toxicosis in cats.

Clinical presentation

In cats, clinical signs of hypersalivation, agitation, tachypnoea, weakness, vomiting, tremors, seizures, secondary hyperthermia and death may occur. Dogs typically do not develop CNS or systemic signs; rather, adverse effects of dermal paraesthesia ('tingling' sensation), pruritus, rubbing, chewing/biting, anxiety, hiding and panting may be seen.

Diagnostics

Haematology, serum biochemistry and urinalysis could be considered to rule out other causes of tremors or seizures. Hypoglycaemia, myoglobinuria and evidence of DIC may be seen due to persistent tremors or seizures.

Treatment

On presentation, any signs of tremoring or seizuring should be treated immediately. Immediate intravenous access should be established and a muscle relaxant (e.g. methocarbamol) or anticonvulsant (e.g. phenobarbital, benzodiazepine) given. Following neurological stabilization, dermal decontamination should be performed. Washing up liquid or degreasing soap must be used appropriately to remove the oily product from the skin. Supportive care and symptomatic treatment, including intravenous fluid therapy, thermoregulation, blood glucose monitoring and continued drug administration (e.g. muscle relaxants, anticonvulsants), should be continued until signs resolve (1–3 days). In dogs, paraesthesia should be treated with dermal decontamination. Cool compresses and topical vitamin E ointment may also relieve clinical signs of paraesthesia. As paraesthesia is not a hypersensitivity reaction, treatment with antihistamines and corticosteroids is not necessary.

Prognosis

The prognosis is excellent with 2–3 days of supportive care in an intensive care unit.

Macrocyclic lactones

Description and exposure

Macrocyclic lactones such as ivermectin, moxidectin and selamectin are commonly used as veterinary antiparasitic medications. Toxicosis occurs when small animals ingest a high dose (e.g. in the form of a large animal deworming product such as equine dewormer), or at lower doses in breed-sensitive dogs (e.g. ABCB1-1Δ polymorphism of P-glycoprotein 1 in breeds such as Border Collies and Australian Shepherd Dogs).

Mechanism of action

Ivermectin stimulates the release and binding of GABA, which blocks electrical activity in nerves and muscle fibres. A subsequent influx of chloride results in hyperpolarization and neuromuscular paralysis.

Clinical presentation

In dogs with ivermectin toxicosis, mydriasis can be seen at lower doses (<2.5 mg/kg), while tremors can be seen at 5 mg/kg. At higher doses (>10 mg/kg), seizures, coma and hypoventilation can be seen. Death has been reported at doses >40 mg/kg. Sensitive dog breeds with ABCB1-1Δ polymorphism can show signs at 0.1 mg/kg; note that the LD_{50} is only 0.15–0.2 mg/kg in sensitive dogs. Adult cats seem to tolerate macrocyclic lactones at a dose of 0.75 mg/kg orally before clinical signs are seen.

Diagnostics

Serum levels of ivermectin can be measured at some reference laboratories; however, there is typically a significant delay until results are available.

Treatment

Treatment involves symptomatic and supportive care. The half-life of different macrocyclic lactones varies between 3.3 and 26 days so it is important to warn the owner that supportive care may be necessary for days to weeks.

Decontamination (including gastric lavage and multiple doses of activated charcoal), antiemetic therapy (to prevent secondary aspiration), intravenous fluid therapy, thermoregulation, anticonvulsant therapy, muscle relaxants, nutritional support, nursing care and monitoring of appropriate oxygenation and ventilation with potential institution of mechanical ventilation should be considered, especially in the acute phase of the toxicosis. In severe acute cases, the use of ILE can be considered for the treatment of ivermectin toxicosis (Clark *et al*., 2011). However, response is variable and not all patients may respond. Patients that are homozygous for the ABCB1-1Δ mutation have not been reported to respond well to ILE therapy (Wright *et al*., 2011).

Prognosis

Most patients require intensive care and prolonged hospitalization. Prognosis is fair to guarded, as treatment (including mechanical ventilation) may be cost-prohibitive.

Chocolate and caffeine

Description and exposure

Chocolate is a very common toxicant that contains methylated xanthine alkaloids (e.g. theobromine, caffeine). Dogs may also be exposed to other potentially dangerous sources of methylxanthines, such as stimulants/caffeine pills, coffee grounds, coffee beans, energy drinks, weight loss supplements and body building supplements.

Mechanism of action

Methylxanthines work by inhibiting cellular phosphodiesterase (increasing cyclic adenosine monophosphate (cAMP)), stimulating catecholamine release, increasing calcium entry into muscle cells and competitive inhibition of adenosine.

Clinical presentation

Clinical signs often include agitation, vomiting, diarrhoea, polyuria, polydipsia, tachycardia, arrhythmias (e.g. supraventricular tachycardia, ventricular premature complexes), ataxia, tremors and seizure activity. Death is possible at very high doses, due to secondary complications (e.g. aspiration pneumonia, DIC).

Diagnostics

Bloodwork abnormalities seen with methylxanthines include hypokalaemia and/or hyperglycaemia and hypoglycaemia. Blood pressure measurement and electrocardiography are important monitoring and diagnostic tools in symptomatic patients.

Treatment

Aggressive decontamination, including emesis induction, is recommended. Chocolate can remain in the stomach for prolonged periods of time; therefore, emesis can be induced up to 6 hours following exposure. Gastric emptying should be considered with caution in patients that are already symptomatic (e.g. if neurologically inappropriate or cardiovascularly unstable). Multiple doses of activated charcoal, without a cathartic, should be given every 6 hours for 24 hours due to enterohepatic circulation. Intravenous fluids, anxiolytics (e.g. phenothiazines), beta-blockers, muscle relaxants and anticonvulsants may all be indicated depending on the severity of signs. Methylxanthines are absorbed by the bladder epithelium, so frequent walks to encourage frequent urination are important while hospitalized.

Prognosis

Excellent with supportive care.

Xylitol

Description and exposure

Xylitol is a natural, sugar-free sweetener commonly found in diabetic chewing gum, calorie-free products (e.g. chewing gum, snacks, foods, sweets), chewable multivitamins, OTC or prescription supplements and medications, food products (e.g. baked goods, peanut butter) and common household products (e.g. nasal sprays, mouthwashes and toothpastes).

Mechanism of action

In non-primate species, xylitol results in an insulin spike within 15–30 minutes of ingestion that causes severe hypoglycaemia. In dogs, doses as low as 0.05–0.1 g/kg have been associated with hypoglycaemia. With higher doses (>0.5 g/kg), acute hepatic necrosis can be seen (Dunayer and Gwaltney-Brant, 2006). Anecdotally, the ASPCA Animal Poison Control Center reports cases of acute hepatic necrosis with as little as 0.25 g/kg of xylitol.

Clinical presentation

Patients typically present with clinical signs of hypoglycaemia, including lethargy, vomiting, weakness, collapse, tremors and seizures. In patients ingesting hepatotoxic doses, clinical signs of malaise, melaena, icterus, GI distress, lethargy, collapse, coagulopathy, altered mentation (secondary to hepatic encephalopathy) and seizures may be seen.

Diagnostics

On initial presentation, blood glucose levels should be measured immediately prior to emesis induction. With toxic ingestions, frequent blood glucose monitoring is recommended. In patients ingesting a potentially hepatotoxic dose, baseline haematology and biochemistry should be performed. If hepatotoxicity occurs, clinicopathological changes may include the following: hyperbilirubinaemia, elevated liver enzymes, hypoglycaemia, hypoalbuminaemia, hypocholesterolaemia, decreased blood urea nitrogen, hyperammonaemia and prolonged clotting times.

Treatment

Hypoglycaemic patients should receive an immediate bolus of 50% dextrose (1 g/kg), diluted with an equal volume of 0.9% NaCl or lactated Ringer's solution (given intravenously over 1–2 minutes). Once the patient has been stabilized and is normoglycaemic, induction of emesis can be considered if a large wad of gum is suspected to have formed a bezoar in the stomach. Activated charcoal does not need to be administered to animals with xylitol toxicosis, as it does not bind reliably. In hypoglycaemic patients, additional supplementation with a CRI of dextrose (2.5–5% dextrose in isotonic crystalloid maintenance fluids) should

be continued for 12–24 hours until blood glucose stabilizes. Patients that have ingested a dose considered to be hepatotoxic (>0.25–0.5 g/kg) should be treated with hepatoprotectants (e.g. SAMe, NAC, silybin/milk thistle; see Figure 19.10), supportive care and monitoring of liver enzyme concentrations.

Prognosis

With hospitalization and supportive care, the outcome is fair. Liver failure is less common due to pet owner awareness, but can be severe and potentially fatal.

Antidepressants

Description and exposure

SSRIs or selective noradrenaline (norepinephrine) reuptake inhibitors (SNRIs) are commonly prescribed antidepressants.

Mechanism of action

SSRIs work by blocking the reuptake of serotonin in the synapse, resulting in increased levels of serotonin in the presynaptic membrane. Markedly increased levels of serotonin can lead to 'serotonin syndrome', which is characterized by severe cardiovascular and neurological signs and can be life-threatening (Boyer and Shannon, 2005).

Clinical presentation

Clinical signs of SSRI toxicosis include those of serotonin syndrome such as sedation, CNS stimulation, lethargy, anorexia, tachycardia, hypertension, tremors and seizures.

Diagnostics

In severely affected patients, a biochemistry panel and urinalysis should be performed to monitor for hypoglycaemia and myoglobinuria (secondary to tremoring or seizuring).

Treatment

Clinical signs can be seen rapidly with SSRI antidepressant ingestion, therefore induction of emesis at home by pet owners is typically not recommended. Patients should be decontaminated as soon as possible by the veterinary surgeon, provided the patient is asymptomatic. Gastric lavage may be the best option in neurologically inappropriate or severely affected patients. Activated charcoal can be given orally or administered through an orogastric tube. Signs of CNS stimulation (e.g. agitation, aggression) and concurrent tachycardia and/or hypertension should be treated with sedation (e.g. phenothiazines). If persistent tachycardia or hypertension occur, the use of beta-blockers may be necessary; drugs used for treatment of cardiac signs are summarized in Figure 19.12. Blood pressure monitoring and electrocardiography are recommended, along with symptomatic and supportive care.

Prognosis

Outcome is excellent with supportive care.

Grapes, raisins and sultanas

Description and exposure

Grapes and raisins are generally considered nephrotoxic to dogs (Eubig *et al*., 2005). Fruit, cooked products (e.g. baked goods, trail mix) and liquid sources (e.g. grape juice) are considered toxic, although there have been no reports of toxicosis from grapeseed extract.

Drug	Dose	Indication
Atropine	0.02–0.04 mg/kg i.m., i.v. as needed	Bradycardia
Glycopyrrolate	0.01–0.02 mg/kg s.c., i.m. or 0.005 mg/kg i.v. as needed	Bradycardia
Lidocaine	Dogs: 2–4 mg/kg i.v. bolus (maximum 8 mg/kg), then 25–80 µg/kg/min CRI Cats: 0.25–0.5 mg/kg i.v. bolus, then 10–20 µg/kg/min CRI	Ventricular tachycardia. Use with caution in cats due to the risk of neurotoxicity
Procainamide	Dogs: 2–4 mg/kg i.v. bolus, repeated to maximum cumulative dosage of 20 mg/kg, then 10–40 µg/kg/min CRI Cats: 1–2 mg/kg slow i.v., then 10–20 µg/kg/min CRI	Ventricular tachycardia
Verapamil (calcium channel blocker)	Dogs: 0.05 mg/kg i.v., then 2–10 µg/kg/min CRI Cats: 0.025 mg/kg slow i.v., then 2–10 µg/kg/min CRI	Supraventricular tachycardia
Diltiazem (calcium channel blocker)	Dogs: 0.05–0.15 mg/kg slow i.v. up to 0.1–0.3 mg/kg total or 0.5–2 mg/kg orally q8h Cats: 0.25 mg/kg i.v. bolus over 2 min up to a total dose of 0.75 mg/kg or 1–2.5 mg/kg orally q8h (standard release)	Tachycardia
Esmolol (beta-blocker)	250–500 µg/kg slow i.v. over 2 min, then 10–200 µg/kg/min CRI	Tachycardia
Propranolol (beta-blocker)	Dogs: 0.02 mg/kg slow i.v. up to 0.1 mg/kg i.v. or 0.1–0.2 mg/kg orally q8h Cats: 0.02 mg/kg slow i.v. up to 0.1 mg/kg i.v. or 2.5 mg total dose per cat q8–12h	Tachycardia
Amlodipine (calcium channel blocker)	Dogs: 0.1–0.5 mg/kg orally q12–24h Cats: 0.625–1.25 mg total per cat orally q24h	Vasodilation for the treatment of hypertension. Use cautiously in patients with cardiac or hepatic disease. Do not use in hypotensive patients or those with toxicants that may result in hypotension (e.g. calcium channel blockers, beta-blockers)
Hydralazine	Dogs: 0.5–3 mg/kg orally q12h Cats: 2.5 mg total per cat orally q12–24h	Vasodilation

19.12 Recommended cardiac medication. CRI = constant rate infusion.

Mechanism of action

Currently unknown.

Clinical presentation

Vomiting is often the first sign to develop; lethargy, anorexia, abdominal pain, diarrhoea, dehydration, polyuria, polydipsia and uraemic breath may also be observed (typically >24 hours post-exposure).

Diagnostics

Serum biochemistry (specifically a renal panel) and urinalysis (prior to fluid administration) should be performed on initial presentation. Recheck bloodwork to assess renal function should be performed every 24 hours while hospitalized.

Treatment

While previous reports of toxic doses exist in the veterinary literature (Eubig *et al*., 2005), this toxicosis is more recently considered to be potentially idiosyncratic in some dogs. While not all dogs are clinically affected because of the idiosyncratic nature of the nephrotoxicant, aggressive decontamination in the majority of patients is still recommended. Induction of emesis can be attempted several hours after exposure, as these products stay in the stomach for a prolonged period of time. Following emesis induction, a dose of an antiemetic and one dose of activated charcoal should be administered. Depending on the success of emesis, aggressive intravenous fluids (4–10 ml/kg/h), antiemetics and gastroprotectants are recommended. Blood pressure monitoring, urine output and point-of-care bloodwork should be performed while hospitalized, as azotaemia with hypercalcaemia and hyperphosphataemia can be seen within 24 hours. Anecdotally, most dogs that are treated aggressively never develop AKI and are successfully discharged 24–48 hours after the initiation of treatment.

Prognosis

Dogs that develop AKI with oliguria or anuria have a poor to guarded prognosis.

Conclusion

In veterinary medicine, the primary treatment for toxicant exposure should be decontamination and detoxification. As few toxicants have an antidote, treatment of the poisoned patient should be aimed at decontamination and symptomatic supportive care, including fluid therapy, GI support, CNS support, sedation and reversal agents, hepatoprotectants and antidotal therapy (if available). With aggressive supportive care and treatment, the prognosis can be fair to excellent in the veterinary poisoned patient.

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Useful website

Demonstration of gastric lavage:
http://vetgirlontherun.com/veterinary-continuing-education-how-perform-gastric-lavage-dog-vetgirl-video/

Chapter 20

Cardiopulmonary resuscitation

Edward Cooper and Manuel Boller

Cardiopulmonary resuscitation (CPR) continues to command a great deal of interest because of its catastrophic nature, the development of new treatment and monitoring modalities, and the natural aversion to death.

Cardiopulmonary arrest (CPA) is defined as an abrupt cessation of spontaneous and effective ventilation and systemic perfusion (circulation), which leads to cessation of oxygen delivery to tissues followed by death, if not reversed in a timely manner. Common causes in veterinary medicine include anaesthetic overdose, trauma with or without exsanguination, acute cardiac failure from cardiac arrhythmias or myocardial disease (cardiomyopathy, valvular insufficiency), and debilitating diseases such as sepsis.

Even though initially successful resuscitation rates (return of spontaneous circulation (ROSC)) may be around 40% in dogs and cats, CPA currently leads to survival rates in the low single digits, with the exception of animals arresting while under anaesthesia (Kass and Haskins, 1992; Wingfield and Van Pelt, 1992; Hofmeister *et al*., 2009). In fact, current epidemiological data suggest that almost every dog and cat that experiences a CPA in the hospital (other than during anaesthesia) does not survive to hospital discharge (Hofmeister *et al*., 2009); in contrast, survival is approximately 20% in humans experiencing CPA in hospital.

Despite many differences between humans and dogs or cats, this discrepancy suggests that cardiac arrest could be survivable for a considerably higher proportion of veterinary patients. Many barriers to more successful management of small animal CPA exist, including limitations in providing costly post-cardiac arrest (PCA) intensive care in the face of an uncertain outcome.

In order to reduce mortality due to CPA, it is beneficial to think of CPR as a comprehensive management strategy that reaches from prevention/preparedness measures, through basic and advanced life support, to PCA care (Boller *et al*., 2012). The goal of the Reassessment Campaign on Veterinary Resuscitation (RECOVER) initiative was to describe how best to execute such a comprehensive strategy in dogs and cats by providing a single set of consensus- and evidence-based CPR guidelines (Fletcher *et al*., 2012). These guidelines were generated after conducting a systematic literature review to answer the most pertinent clinical questions on how best to perform CPR in dogs and cats (Boller and Fletcher, 2012). RECOVER addressed five key areas of CPR:

- Preparedness and prevention
- Basic life support (BLS)
- Advanced life support (ALS)
- Monitoring
- PCA care.

This chapter will provide the most important principles and guidelines on small animal CPR.

Preventative measures

The poor prognosis for animals with CPA demands that its prevention is of highest priority. An effective resuscitation strategy begins by identifying patients at risk of CPA during their hospitalization. Regular cage-side rounds including all veterinary care providers, especially nurses, allow effective recognition of patients at risk of CPA across the whole clinical team. A list of potential causes of CPA that are reversible, also known as the 5Hs and 5Ts, can help to identify patients at risk (Figure 20.1). Moreover, a monitoring and response protocol appropriate for the perceived risk factors of an individual patient should be implemented to identify any worsening of the patient's condition in a timely manner. This then allows correction of life-threatening abnormalities before CPA occurs.

To use the example of a dog with a partial upper airway obstruction, preparing equipment required for endotracheal intubation (e.g. endotracheal tubes of various sizes, laryngoscope and sedatives) and locating these items in proximity to the patient at risk will allow rapid intervention in case of deterioration. In animals at risk of CPA, planned diagnostic or therapeutic procedures, e.g. those requiring sedation or anaesthesia, should be adjusted or delayed as permissible. Referral to a veterinary facility that can provide 24-hour critical care may be required to minimize the risk of CPA.

5Hs
• Hypovolaemia/haemorrhage • Hypoxia/hypoventilation • Hydrogen ions (acidosis) • Hyperkalaemia/hypokalaemia • Hypoglycaemia
5Ts
• Toxins • Tension pneumothorax • Thromboembolism (PTE)/thrombosis • Tamponade (pericardial effusion) • Trauma

20.1 The 5Hs and 5Ts that list reversible causes of cardiopulmonary arrest. PTE = pulmonary thromboembolism.

Preparedness measures

An in-hospital 'chain of prevention' has been proposed in human medicine to optimize the level of preparedness and the quality of the response to a CPA event (Smith *et al.*, 2010). The five basic elements of this preparedness strategy are:

- Staff education
- Patient monitoring
- Risk recognition
- The call for help
- The response.

Education should focus on both recognition of patients at risk of CPA (as described above) and the response to CPA and technique of CPR. CPR training, which should include both didactic training to convey theoretical knowledge on CPR and hands-on practice, is the foundation for resuscitation success. Evidence suggests that refresher training every 6 months is required to reduce skill degradation. Debriefing sessions following every resuscitation should occur to analyse and discuss team performance and hence, improve the quality of future resuscitations.

Monitoring equipment and monitoring skills are important for:

- Identification of patients at risk of CPA
- Identification of patients in CPA
- Guidance of ALS interventions during CPR
- Titration of PCA care.

Given the numerous responsibilities, execution of high-quality ALS ideally involves at a team of at least three rescuers. As such, a plan should be in place to call for help effectively in case of a CPA.

To optimize the response to CPA, an easily accessible, audited crash cart (Figure 20.2) containing all required drugs, tools and equipment (Figure 20.3), including a defibrillator, should be available. Staff should be trained in the correct operation of equipment such as monitoring devices, defibrillator and suction unit. In addition, cognitive aids (e.g. CPR algorithm and drug dosing chart) should be displayed in the resuscitation area, and hospital staff should be made familiar with the use of these aids at regular intervals.



20.2 Crash cart, including defibrillator, drugs, endotracheal tubes of various sizes, syringes, needles and catheters, manual resuscitator (Ambu) bags, and surgical sets for thoracotomy and surgical haemostasis.

Establishing a CPR directive

In addition to general preparedness to perform CPR, an essential component of preparedness is establishing an appropriate directive (resuscitation code status) for each patient, especially those at increased risk for CPA (e.g. patients that are critically ill or undergoing anaesthesia). It is therefore extremely important to have an informed discussion with the owner regarding their options, prior to development of CPA, whenever possible. While at times unpleasant, informing the client that CPA is possible and speaking frankly about the potential success of CPR (which may depend on the patient population) can help to avoid unnecessary or fruitless efforts. In most clinical settings the potential resuscitation codes offered include 'do not

Drugs

Required:
- Adrenaline (epinephrine)
- Vasopressin
- Atropine
- Lidocaine
- Calcium gluconate
- 50% dextrose
- Isotonic crystalloids (e.g. 0.9% NaCl, lactated Ringer's solution)

May be useful:
- Amiodarone
- Magnesium sulphate
- Furosemide
- Mannitol
- Sodium bicarbonate
- Diazepam/midazolam
- Hypertonic saline
- Naloxone

Equipment

- Pressure bag for rapid fluid infusion
- Manual resuscitator (Ambu) bag
- Endotracheal tubes (various sizes)
- Laryngoscope
- Isopropyl alcohol
- Antiseptic scrub
- Hypodermic needles (various sizes)
- Intravenous catheters (various sizes)
- Gauze sponges/swabs (2 inches x 2 inches (5 x 5 cm), 4 inches x 4 inches (10 x 10 cm))
- Tape (½ inch (1.2 cm), 1 inch (2.5 cm), 2 inches (5 cm))
- Roll of gauze (2 inches (5 cm))
- Polyethylene urinary catheters
- Suture material
- Three-way stopcocks
- Thoracotomy tray with loaded scalpel blade
- Clippers
- Electrocardiogram (ECG) monitor/defibrillator
- Capnograph
- External and sterile internal defibrillator paddles
- Intraosseous cannula placement device and intraosseous cannula
- Set-up airway suctioning device (ready to use)

Other

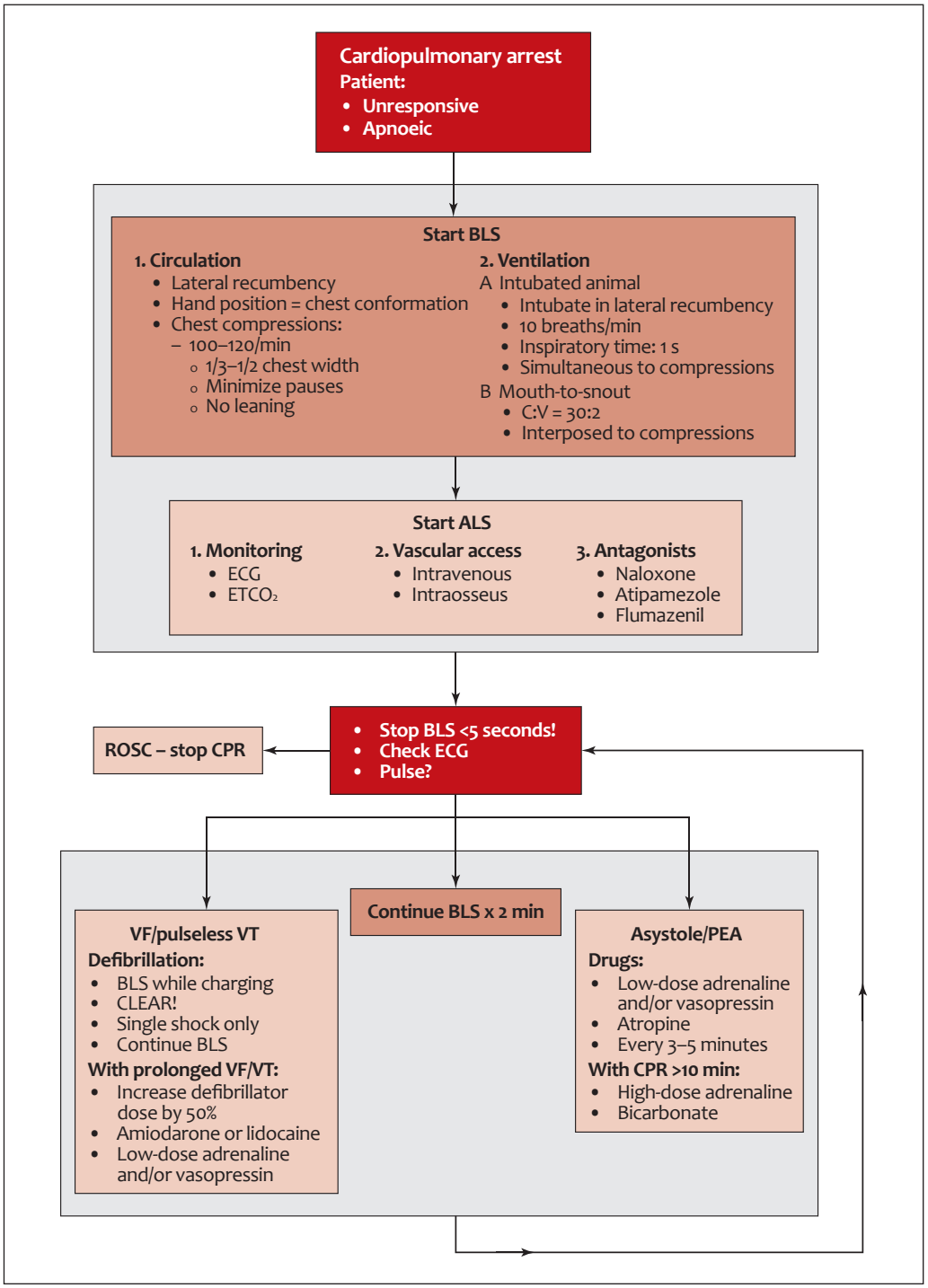
- Emergency drug dosing chart
- CPR algorithm poster

20.3 Crash cart drugs and equipment.

resuscitate'; 'do resuscitate'; or 'do resuscitation with open-chest CPR if indicated'. It is generally reasonable to encourage efforts to perform CPR in patients undergoing anaesthesia as these have the highest potential for successful outcome. However, for patients with severe/terminal disease processes (cardiac, renal, neurological) the discussion might be more appropriately focused on acknowledging the low chance of survival to discharge and recommending against heroic efforts. Just because CPR can be done, does not always mean that it should. If no discussion takes place, the default directive in most clinical circumstances is to perform CPR, which may not be in the best interest of the patient or the owner. As such, availability of the patient's code status will allow for optimal and appropriate rescuer response to CPA.

Recognition of cardiopulmonary arrest and initiation of cardiopulmonary resuscitation

Early recognition of CPA and timely response are of great importance for a satisfactory outcome. Thus, the diagnosis of CPA should be made after only a short and focused assessment lasting no more than 10–15 seconds. The clinical criteria to identify a non-anaesthetized patient with CPA are the presence of unconsciousness and apnoea (Figure 20.4). Hence, any non-anaesthetized, acutely unresponsive patient that is not breathing should immediately



20.4 Cardiopulmonary resuscitation (CPR) algorithm. Basic life support (BLS) is started immediately after recognition of cardiopulmonary arrest (CPA), continued throughout the resuscitation effort and only interrupted every 2 minutes for short patient evaluations (electrocardiogram (ECG) and pulse). Advanced life support (ALS) measures occur whilst BLS is ongoing.
C:V = compression:ventilation;
$ETCO_2$ = end-tidal carbon dioxide;
PEA = pulseless electrical activity;
ROSC = return of spontaneous circulation;
VF = ventricular fibrillation;
VT = ventricular tachycardia.

undergo a very succinct examination, including a rapid evaluation of airway, breathing and circulation (ABC). Importantly, if any doubt about the presence of CPA remains, CPR should be started immediately, as opposed to spending time applying further, advanced or time-consuming diagnostic methodologies.

There are several reasons for this 'streamlined' approach. First, pulse palpation is insensitive and lacks specificity in human CPR, and probably lacks specificity in small animals as well. Thus, the assessment of an arterial pulse is no longer included as a necessity for diagnosis of CPA. Second, a delay in initiation of CPR will negatively affect the outcome (Herlitz *et al*., 2002). Finally, the risk associated with applying CPR to the rare patient falsely diagnosed with CPA is minimal.

Occasionally, CPA occurs in patients that are sedated or under general anaesthesia and under these circumstances, unconsciousness and apnoea may not be practical criteria to identify CPA. Thus, other physiological parameters must be used to indicate impending or actual CPA, and appropriate monitoring should be in place. These parameters could include assessment of heart or pulse rate (electrocardiography, pulse oximetry, oesophageal stethoscope, direct arterial blood pressure, Doppler sphygmomanometry), blood flow (capnography, Doppler sphygmomanometry) or continuous blood pressure (direct arterial blood pressure). Any abnormality indicative of CPA, such as a sudden decrease in end-tidal carbon dioxide ($ETCO_2$) concentration, sudden decrease or loss of Doppler signal, decrease in arterial blood pressure, or alteration of electrocardiogram (ECG) appearance (severe bradycardia, asystole, severe ventricular arrhythmia or even fibrillation) should be immediately investigated, and the finding cross-referenced with another monitoring modality (e.g. absence of auscultable heartbeat on oesophageal stethoscope), rather than solely troubleshooting the equipment. This assessment should take no longer than 10–15 seconds, and as for the non-anaesthetized patient, CPR measures should be initiated if CPA cannot be excluded at that time.

Basic life support

Once the decision to perform CPR has been made, BLS and ALS should be initiated as rapidly as possible in a sequential, orderly and predetermined manner. High-quality BLS is of the utmost importance for a successful resuscitation from CPA. BLS includes circulatory support (C), provision of effective ventilation by establishing and maintaining an airway (A), and controlling breathing (B). Chest compression and ventilation should be initiated as early as possible, which will frequently lead to earlier administration of chest compression compared with ventilation, given the time and equipment required for the latter. Delay of chest compressions until an airway is established and ventilation initiated is not recommended. Therefore, the resulting C-A-B sequence of BLS interventions will not delay effective ventilation, but lead to earlier provision of chest compressions if several rescuers are present.

If only one rescuer is present, the apparent cause of CPA should dictate priority. With an assumed or witnessed primary cardiac cause, compressions are initiated first (C-A-B), and with an assumed or witnessed primary respiratory CPA, ventilation first (A-B-C) is recommended (Hopper *et al*., 2012). However, there is no evidence in veterinary or human medicine that supports either the C-A-B or the traditional A-B-C approach (Hopper *et al*., 2012).

Importantly, the C-A-B sequence does not devalue the need for early effective intubation and ventilation in veterinary small animal patients with CPA, and is not to be confused with chest-compression-only CPR. Chest-compression-only CPR (i.e. C without the A-B) is reasonable in adult humans with out-of-hospital cardiac arrest if CPR is delivered by untrained bystanders (Kleinman *et al*., 2015). This is based largely on the fact that primary cardiac arrest (e.g. due to ventricular fibrillation) constitutes the most prevalent aetiology of CPA in humans, thoracic compressions produce adequate ventilation and oxygenation for several minutes, and the inhibition of the lay rescuer to deliver mouth-to-mouth ventilation (Berg and Berg, 2012). In contrast, asphyxial CPA is common in small animals, and a chest-compression-only approach leads to worse outcomes in this population (Berg and Berg, 2012). Compression-only CPR is therefore not a recommended strategy for dogs and cats with CPA.

Circulation

The return of effective cardiac electrical and mechanical activity depends upon the early restoration of myocardial oxygenation and blood flow. As such, cardiac/thoracic compressions should be initiated as soon as possible after occurrence of CPA. Even under the best circumstances, the efficacy of closed-chest compressions is limited and may generate only 20–30% of normal cardiac output; the importance of optimal chest compression technique cannot be emphasized enough. The quality of chest compressions is defined by the compression rate and depth, chest recoil between compressions, interruptions of compressions, and the hand location on the patient's chest.

During CPR, blood flow is generated by compressing the patient's chest wall. In cats, small dogs and dogs with keel-shaped chest conformation, blood moves through the heart and vessels during chest compression due to direct cardiac compression (cardiac pump mechanism). In larger dogs with wide or flat chests, phasic decreases and increases in intrathoracic pressure will lead to indirect filling and collapse of intrathoracic large vessels and the heart, leading to expulsion of blood out of the chest into the systemic circulation with each compression (thoracic pump mechanism) (Peters and Ihle, 1990).

These physiological considerations dictate patient posture and rescuer hand position during administration of external chest compressions. It is generally recommended that effective chest compressions are executed with the animal in either right or left lateral recumbency. To take advantage of the cardiac pump mechanism in cats and very small dogs, the rescuer's stronger hand is wrapped ventrally around the sternum, with the thumb and opposing forefingers compressing the chest bilaterally and directly over the heart. The other hand should reach around the animal's back to prevent the patient from moving away from the compressing hand (Figure 20.5). For small dogs (<10 kg bodyweight), compressions should be achieved by placing the palm of the hand (or both hands stacked) directly over the heart.

For medium to large dogs with a round ('barrel') chest conformation, both hands are placed at the widest part of the chest, the goal being to achieve the maximum possible intrathoracic pressure increase with each compression (Figure 20.6). In Greyhounds, Great Danes or other large breeds with a keel-shaped chest conformation, compressions directly over the heart are recommended (Figure 20.7). In flat-chested dogs (e.g. English Bulldogs), sternal compressions with the patient in dorsal recumbency may be a reasonable alternative to latero-lateral compressions (Figure 20.8).



20.5 Hand position in a cat or small dog. One hand stabilizes the back while the other, stronger hand reaches around the sternum to compress the ventral aspect of the thorax between the thumb and opposing digits.



20.6 Hand position in a round-chested dog. Chest compressions occur over the widest part of the chest.



20.7 Hand position in a keel-chested dog. Chest compressions occur over the heart.



20.8 Hand position in a flat-chested dog. The animal is positioned in dorsal recumbency with chest compressions occurring over the sternum.

The body posture of the rescuer is important to increase the effectiveness of compressions and decrease fatigue. The rescuer's arms should be held straight with the elbows locked and the shoulders positioned vertically over the hands, using the entire upper body (rather than just the arms) to deliver compressions (Figure 20.9). If the table is too high for the rescuer to assume the required position, a foot-stool should be used; the rescuer can kneel on the table if considered safe, or the patient can be moved to the floor. It is also recommended that the person delivering chest compressions stands at the dorsal side of the animal, as this will help to stabilize the patient on the table and will allow unobstructed access by other members of the resuscitation team to the patient (e.g. for vascular access).

The ideal chest compression rate in dogs and cats is not known, but is believed to be approximately 100–120 compressions per minute, devoting equal time to compression and relaxation. Significantly slower rates (60 per minute) have been shown to be associated with worse outcomes in an experimental canine model (Feneley *et al*., 1988). Faster than recommended rates could result in incomplete recoil of the chest, with diminished cardiac filling and compromised compression depth. It is recommended that compression depth should be approximately 35–50% of the width of the chest (Hopper *et al*., 2012). In addition, it is important to allow for complete recoil of the chest in between compressions to allow for more effective venous return and cardiac filling.

Application of interposed abdominal compressions (IAC) appears to be another effective means of improving blood flow during CPR, and it is reasonable to apply IAC during CPR if a sufficient number of adequately trained personnel is available (Fletcher *et al*., 2012). IAC is accomplished by



20.9 Posture of rescuer for delivery of chest compressions. The shoulders are positioned vertically over the compression site, the elbows are locked and force is transmitted to the chest via the heels of the hands. Compression force is generated by the core musculature and not the arms.

having a second person apply abdominal pressure during the relaxation phase of chest compressions. Coordination of this effort is important, as simultaneous chest and abdominal compression could be counterproductive. A meta-analysis of experimental studies involving dogs and pigs concluded that this method, if well executed, was effective in increasing cardiac output, blood pressure and cerebral blood flow (Babbs, 2003). While there is theoretical concern for organ damage with IAC, this has not been demonstrated in the literature.

Each interruption in chest compressions will lead to diminished coronary and cerebral perfusion, with increased potential for ischaemia–reperfusion injury. Minimizing such pauses is therefore an explicit part of high-quality CPR. It is recommended that BLS should be performed in 2 minute cycles, avoiding the temptation to perform more frequent interruptions of compressions to assess for ROSC. At the end of the 2 minute cycle, chest compressions will be halted for 3–5 seconds, for ECG analysis and to assess the patient for signs consistent with ROSC. Given the potential for rescuer fatigue and associated decreased effectiveness of chest compressions, it is advisable to alternate providers after every 2 minute CPR cycle.

Airway

As previously discussed, compression-only CPR is not recommended in dogs and cats, and so an essential step in performing CPR is the establishment of a secure and patent airway. The most effective way to achieve this is by endotracheal intubation with a cuffed endotracheal tube. Ideally, efforts to intubate should be made at the same time that chest compressions are performed, with the patient in lateral recumbency with the head and neck extended. Proficiency in intubation in lateral recumbency can be obtained by practising in routine anaesthesia patients. Recognizing that lateral recumbency and movement during chest compressions may increase the difficulty of intubation, if efforts remain unsuccessful the patient can be moved to a sternal position to facilitate placement. Accumulation of fluid/secretions in the oropharynx may necessitate the use of suction to allow for better visual assessment of the larynx and improve the likelihood of successful intubation. Given the stressful and fast-paced nature of CPR, there is significant potential for oesophageal intubation to occur. It is therefore important to verify correct tracheal placement by a combination of direct visual assessment, breath auscultation or use of $ETCO_2$. In the event of a complete or near-complete airway obstruction, peroral endotracheal intubation might not be feasible, in which case emergency tracheostomy should be performed (see Chapter 7).

If endotracheal intubation is not immediately available or possible (such as with a single responder), it may be necessary to consider mouth-to-snout or bag-mask ventilation. The evidence in support of these techniques is limited, but they may be sufficient to allow oxygenation and ventilation during the initial stages of CPR (Hopper *et al*., 2012). First, clearance of foreign bodies or fluids from the oropharyngeal area needs to be ensured. Mouth-to-snout ventilation is then accomplished by firmly closing the animal's mouth, extending the animal's neck such that the nose, neck and back are positioned in a straight line, and placing the rescuer's mouth on the patient's nose such that an airtight seal results. Bag-mask ventilation may require specialized equipment in order to achieve an adequate seal for effective ventilation. Inflation of the stomach with air may occur with either technique. Importantly, for effective ventilation and to reduce gastric inflation, chest compressions need to be interrupted during breath delivery. This requirement will compromise the effectiveness of BLS. Ventilation via an endotracheal tube does not demand pauses in chest compressions and is therefore preferred.

Breathing

The primary goal of ventilatory support during CPR is to achieve and maintain normocapnia and normoxaemia. Controlled or assisted ventilation can be accomplished by connecting a properly placed endotracheal tube to a self-inflating Ambu bag or anaesthetic machine and delivering 100% oxygen. Ten breaths per minute should be provided in both dogs and cats (approximately 1 breath per 10 compressions), unless very severe pulmonary parenchymal disease is present. If the latter is believed to be the case, more frequent ventilation (15–20 breaths per minute) may be indicated. Numerous studies have shown that higher and lower ventilation rates can be associated with worse outcomes, as described below (Cavus *et al*., 2008; Lurie *et al*., 2008). The size of each breath (tidal volume) delivered should approximate 10 ml/kg at a maximum peak inspiratory pressure of 20–25 cmH_2O. This volume generally results in visible but minimal expansion of the chest or movement of the abdomen, but this can be difficult to assess while chest compressions are being performed.

Poor training and the excitement associated with CPR can often lead to higher than recommended ventilation rates. This should be avoided as it can be harmful for a number of reasons. Hypocapnia associated with hyperventilation can lead to decreased cerebral perfusion from reflex vasoconstriction, thereby worsening neuronal injury. In addition, experimental studies in pigs have demonstrated that hyperventilation during CPR is associated with lower coronary and cerebral perfusion pressures and reduced survival (Aufderheide and Lurie, 2004; Cavus *et al*., 2008). The overall duration and extent of positive intrathoracic pressure generated by positive pressure ventilation during CPR is responsible for these negative effects, as it impedes venous return and cardiac filling and hence reduces the amount of blood flow generated by the subsequent chest compression. For the same reason, ventilation with positive end-expiratory pressure should be avoided.

In addition to standard ventilation, there has been considerable investigation into the manipulation of airway pressure to augment cardiac filling during the relaxation phase of chest compressions. An impedance threshold device (ITD) attaches to the endotracheal tube and prevents inflow of air during chest recoil. This serves to increase the amount of negative intrathoracic pressure during chest recoil and promotes venous return. Experimental studies in dogs and pigs have shown promising improvement in haemodynamics during CPR (Buckley *et al*., 2012; Metzger *et al*., 2012), but human studies have failed to show a survival benefit (Aufderheide *et al*., 2011). However, given that there is no evidence to suggest a harmful effect, use of an ITD warrants consideration in patients >10 kg bodyweight.

Advanced life support

ALS includes monitoring, vascular access, drug therapy, defibrillation and open-chest CPR (OC–CPR) and occurs after BLS has been initiated. ALS is superimposed on to

ongoing BLS. As such, ALS interventions are considered adjuncts to BLS and should be executed in a way that minimally affects the quality of chest compressions and ventilation.

Monitoring

Most haemodynamic monitoring techniques used in medical practice are designed to work in patients with a spontaneously beating heart and intact circulation, but will cease to provide meaningful measurements during CPR. In addition, motion artefacts will further limit the usefulness of many devices. Specifically, pulse oximetry, oscillometric or Doppler blood pressure measurement devices may be helpful to monitor the patient at risk of CPA or after ROSC has occurred, but are of little use during CPR. In contrast, electrocardiography and capnography are useful monitoring modalities during CPR, and the current RECOVER guidelines recommend their use (Fletcher *et al*., 2012).

Electrocardiography

ALS interventions, such as the drug regimen or defibrillator use, are influenced by knowledge of the heart rhythm (Figure 20.10). Electrocardiography is therefore an essential monitoring modality to convey that information. Unfortunately, the susceptibility of a conventional ECG for motion artefacts is significant, such that a meaningful rhythm analysis cannot be obtained during ongoing chest compressions. Hence, chest compressions need to be paused for rhythm analysis. To minimize interruption of chest compressions, ECG analysis should be limited to 3–5 seconds between each 2 minute cycle of BLS.

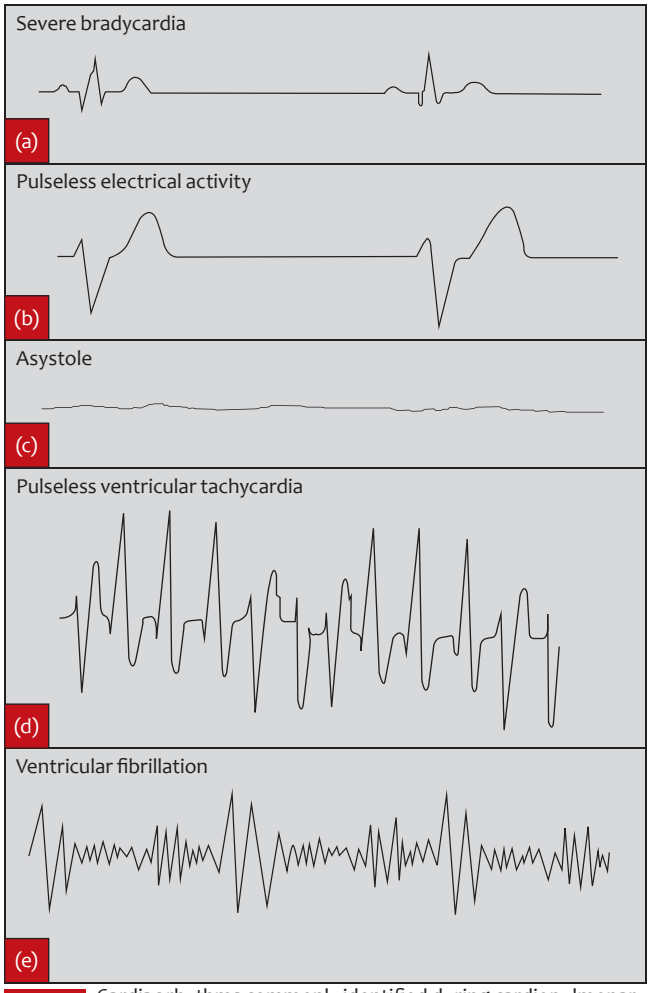
The most common arrest rhythms initially encountered in dogs and cats with CPA are pulseless electrical activity (PEA), asystole, or ventricular fibrillation (VF)/pulseless ventricular tachycardia (VT). A lack of any cardiac electrical activity always indicates cardiac arrest. The reverse, however, is not always true. A normal ECG does not ensure that cardiac contractile function is adequate to generate an appreciable pulse, or a meaningful amount of peripheral blood flow.

PEA is a catch-all term used to describe patients that have electrocardiographic evidence of an organized cardiac rhythm paired with absence of both a palpable peripheral arterial pulse and signs of clinically appreciable circulation. Patients may or may not have an auscultable heartbeat. Clinically, if direct arterial blood pressure is measured, an arterial blood pressure oscillation may be identified, but at a very low level (e.g. systolic arterial blood pressure below 40 mmHg). Potential causes include anaesthetic overdose, acute hypoxia, severe acidosis, systemic toxicity, severe electrolyte abnormalities (e.g. hyperkalaemia), cardiogenic shock, massive pulmonary thromboembolism, tension pneumothorax and more. PEA is a non-shockable rhythm which means that defibrillation will not be effective in restoring spontaneous circulation. Treatment involves addressing the underlying cause(s), and the administration of vasopressors (adrenaline (epinephrine), vasopressin), atropine or, after prolonged CPA, bicarbonate (see Figure 20.4).

Ventricular asystole has a distinctly different ECG appearance from any other arrest rhythm, in that it is devoid of any electrical activity. Like PEA, asystole is a non-shockable rhythm. External electrical defibrillation is only required if asystole progresses to ventricular fibrillation (VF).

In humans, sudden CPA outside of the hospital most often follows myocardial infarction, with VF being a frequent arrest rhythm. Human arrests in hospital, however, often have other triggers and more closely mirror what happens in canine and feline CPA. Consequently, VF is less frequently observed in these populations, and was found to be the first identified rhythm in 17% of humans, 7% of dogs and 2% of cats with CPA (Hofmeister *et al*., 2009; Meaney *et al*., 2010). VF is associated with a better outcome in humans compared with asystole and PEA; however, such data are lacking in the veterinary literature. While VF is not commonly the inciting cause of CPA in small animals, it can evolve from asystole or PEA during the course of CPR. VF is a shockable rhythm and the treatment of choice for VF is transthoracic or internal electrical defibrillation (see below).

Pulseless VT is occasionally observed. Although most of the VT seen in clinical practice occurs as a pulse-generating and perfusing rhythm, it occasionally compromises cardiac output to the extent that a clinical diagnosis of CPA ensues, e.g. the patient becomes unconscious and apnoeic. As this is a shockable rhythm, electrical defibrillation as for VF is the most appropriate treatment.



20.10 Cardiac rhythms commonly identified during cardiopulmonary arrest. (a) Severe bradycardia: very slow heart rate (<30–40 bpm) in conjunction with loss of consciousness and respiratory arrest or agonal breathing, and a palpable pulse. (b) Pulseless electrical activity: slow heart rate in conjunction with loss of consciousness and respiratory arrest or agonal breathing, but without a palpable pulse. (c) Asystole: complete absence of electrical activity. (d) Pulseless ventricular tachycardia: rhythm with repeating complexes of variable regularity and typically very high rate (>250 bpm) in conjunction with loss of consciousness, apnoea or agonal breathing and no palpable pulse. (e) Ventricular fibrillation: chaotic rhythm at a high rate. May occur as coarse (high amplitude) or fine (low amplitude) ventricular fibrillation.

Capnography

$ETCO_2$ monitoring is a safe, non-invasive, feasible and robust technology for use during CPR. Many different bedside capnographs are available or can be found as an integrated part of multiparameter monitoring devices or even in defibrillators. $ETCO_2$ has been used extensively in CPR as it correlates with coronary blood flow and likelihood of ROSC. If ventilation remains constant, $ETCO_2$ may provide real-time physiological feedback on the efficacy of chest compressions delivered. Hence, a low $ETCO_2$ (e.g. <15 mm Hg; (<2 kPa)), should lead to an effort to adjust ventilation technique or to improve quality of compressions, e.g. to press harder, or to change hand position on the chest. A very low $ETCO_2$ value (e.g. <10–15 mm Hg; (<1.5–2 kPa)) has also been associated with reduced likelihood of ROSC in dogs and humans (Hofmeister *et al*., 2009). The marked increase in blood flow associated with ROSC is reflected in a sudden rise in $ETCO_2$ value and can be identified without requiring interruption of chest compressions.

Vascular access

Intravenous access is extremely important for the delivery of medications and potentially intravenous fluids during CPR. For patients that experience CPA without an intravenous catheter in place, vascular access can prove extremely challenging given the low-flow state and venous stasis. While attempts at percutaneous access may be successful, these efforts are likely to result in wasted effort and lost time. Alternately, a vascular cut-down technique or placement of an intraosseous catheter should be considered.

Vascular cut-down can be performed over the cephalic, saphenous or jugular veins. This procedure is covered in greater detail elsewhere (see Chapter 2) but a brief review is provided here. After a quick 'clip and prep' at the desired site, the skin over the vein is moved to the side and a parallel incision made. The skin can then be returned so that the incision is over the vein. Using fine-tipped scissors and/or haemostats and careful dissection, the vein is isolated from the surrounding fascia. A standard intravenous catheter can then be directly inserted into the isolated vessel and secured.

Performing a vascular cut-down may prove to be technically challenging, especially under the stressful circumstances of CPR. Another consideration is placement of an intraosseous catheter (see Chapter 2). Intraosseous catheters have the benefit of providing the equivalent of vascular access and allowing administration of any medication that is normally given intravenously. Typical sites for intraosseous catheter placement include the trochanteric fossa of the femur, greater tubercle of the humerus or the wing of the ilium. For neonates, paediatrics and small patients (<5 kg), use of a hypodermic needle in the trochanteric fossa is often quick and effective. For larger patients, there are multiple options, including use of commercially available intraosseous cannulas, bone marrow aspiration needles or a needle-driver system (e.g. EZ-IO™). With the latter, a small power drill is used to quickly drive a specialized needle system into the desired location.

If neither of these means of access is possible, medications can be administered via the endotracheal route. Generally speaking, the dose needs to be doubled for medications given by this route and diluted with sterile isotonic saline or sterile water at a ratio of 1:1. A long catheter should be passed through the endotracheal tube such that its tip is located beyond the level of the carina to improve effective drug delivery (see specific recommendations below). The catheter should be flushed with sterile 0.9% saline solution at a sufficient volume to clear the drug from the catheter. Intracardiac injection is generally not recommended unless open-chest CPR is performed and the heart is visible.

Drug therapy

The list of drugs commonly used during CPR is quite short, and it is recommended that these medications are kept close to the resuscitation area (e.g. in a crash cart). A dosing chart should be displayed in the resuscitation area to minimize the time required for dose calculation during CPR and to reduce the risk of dosing errors. An example of a dosing chart forms part of the RECOVER small animal CPR guidelines and can be downloaded from the *Journal of Veterinary Emergency and Critical Care* website (http://onlinelibrary.wiley.com/doi/10.1111/j.1476-4431.2012.00757.x/full). Alternatively, a chart can be generated independently using the appropriate dosages (Figure 20.11).

Depending on the underlying arrest rhythm, the assumed cause of arrest, the CPA context and the duration of CPR, administration of vasopressors, anticholinergics, antiarrhythmics, reversal drugs, intravenous fluids or sodium bicarbonate may be indicated as part of ALS.

Vasopressors

The beneficial effect of vasopressors during CPR lies in the redistribution of blood flow from peripheral vascular beds to the 'core circulation' (heart, brain and lungs) via an increase in vascular tone. This is important because only a fraction of normal aortic forward blood flow (e.g. 20–30% of normal cardiac output) is typically generated during closed-chest CPR. Adrenaline is the most extensively

Drug	Indications	Dosage	Action
Adrenaline	Asystole; PEA; prolonged VF or pulseless VT	0.01 mg/kg i.v., i.o. bolus q3–5 min 0.1 mg/kg i.v., i.o. after prolonged arrest 0.02–0.2 mg/kg intratracheally	Vasopressor; alpha- and beta-adrenergic agonist
Amiodarone[a]	VF or pulseless VT resistant to electrical defibrillation	5 mg/kg i.v., i.o.	Class III antiarrhythmic
Atropine sulphate	PEA; asystole; presumed vagal aetiology of cardiopulmonary arrest	0.04 mg/kg i.v., i.o. 0.08 mg/kg intratracheally	Parasympatholytic
Lidocaine	VF or pulseless VT resistant to electrical defibrillation	Dogs: 2 mg/kg i.v., i.o. bolus Cats: 0.25–0.5 mg/kg i.v., i.o. bolus	Class IB antiarrhythmic
Vasopressin	Asystole; PEA; prolonged VF or pulseless VT	0.8 IU/kg i.v., i.o. q3–5 min	Vasoconstriction

20.11 Drugs routinely administered during cardiopulmonary resuscitation. [a] Care advised depending on preparation used as may lead to anaphylaxis. PEA = pulseless electrical activity; VF = ventricular fibrillation; VT = ventricular tachycardia.

studied and most often clinically used vasopressor. Low doses (0.01 mg/kg i.v. or i.o.) and high doses (0.1 mg/kg i.v. or i.o.) of adrenaline have been shown to provide similar survival outcomes, but the adverse effects associated with high doses are more severe. One reason for this may lie in the fact that adrenaline does not only lead to increased peripheral vascular resistance, but will also increase myocardial oxygen consumption and the incidence of ventricular tachyarrhythmias after ROSC. The overall observation in human clinical studies is that the rate of ROSC may be higher after use of high-dose adrenaline, but that a higher proportion of these initial survivors will die during the PCA phase, resulting in no survival benefit.

Administration of low-dose adrenaline is recommended every other cycle (i.e. every 3–5 minutes), with the first administration occurring during the first or second cycle in animals with asystole or PEA, and after the second non-successful defibrillation in animals with VF/pulseless VT as the initially identified CPA rhythm. However, after prolonged CPR (e.g. more than 10 minutes) administration of a high dose of adrenaline can be considered. Endotracheal administration of adrenaline at 2–3 times the intravenous dose can also be considered.

Another increasingly used vasopressor is arginine vasopressin (AVP). The theoretical benefit of AVP is that it acts via a different receptor system from adrenaline, and its activity is much less diminished by acidic environments compared with catecholamines (i.e. adrenaline). Given the severe reduction in tissue pH occurring in the low blood flow state of CPR, this property may convey a more reliable increase in vascular tone. In addition, AVP will be less likely to exacerbate post-ROSC cardiac tachyarrhythmias and increased myocardial oxygen consumption than adrenaline. However, randomized controlled trials in humans have failed to show a clear benefit of AVP over adrenaline, and data from one small veterinary randomized controlled trial in dogs did not support the preferential use of AVP (Buckley *et al*., 2011). Considering the current evidence, vasopressin administration (0.8 IU/kg i.v., i.o. every other cycle of CPR) may be considered interchangeably or in combination with adrenaline.

Anticholinergic drugs

Atropine is an anticholinergic or parasympatholytic drug and its routine administration during CPR may be considered (0.04 mg/kg i.v., i.o. every other cycle of CPR). A stronger recommendation is given for its use in patients with asystole or PEA, and when increased vagal tone may have been responsible for the CPA, as with acute gastrointestinal, respiratory or ocular disease. Atropine can also be administered endotracheally (0.08 mg/kg).

Antiarrhythmic drugs

In patients with VF unresponsive to three or more attempts at defibrillation, administration of antiarrhythmic drugs may be considered in order to increase defibrillation success. The class III antiarrhythmic agent amiodarone has been shown to be the most effective drug in this indication in humans and animals, where it improved defibrillation success compared with standard care (including lidocaine administration) and increased short-term survival (Anastasiou-Nana, 1994; Dorian *et al*., 2002; Somberg, 2002). The dose recommended in dogs and cats is 5 mg/kg i.v. or i.o. as a one-time administration. Conventional amiodarone formulations can cause anaphylactic reactions in dogs, which need to be recognized if occurring after ROSC and treated accordingly, although a new product with different cosolvents may address these concerns (Souney, 2009). Where amiodarone is not available, lidocaine (2 mg/kg i.v., i.o.) administration can be considered instead and can be repeated once at the same dose. Administration of magnesium sulphate (30 mg/kg i.v., i.o.) is not recommended on a routine basis during CPR; however, the use of this drug can be considered in the presence of hypomagnesaemia or torsade de pointes.

In situations where there is no defibrillator available and the patient is in VF, use of these drugs may be warranted. There is no evidence to document their efficacy in this scenario and it is likely to be very low, but in the absence of other options this treatment may be attempted.

Antagonists of sedatives and opioids

In patients that were sedated with reversible drugs, administration of the appropriate antagonist should be considered. These can be administered immediately after vascular access is established since the ECG findings do not guide the use of these drugs. Commonly used antagonists are naloxone (0.04 mg/kg i.v., i.o.) for opioids, flumazenil (0.01–0.02 mg/kg i.v., i.o.) for benzodiazepines, and atipamezole (0.1 mg/kg i.v., i.o.) for alpha-2 adrenoceptor agonists (Figure 20.12).

Intravenous fluids

While CPA is evidently the most severe form of circulatory collapse, routine administration of large volumes of intravenous fluids during CPR is not recommended as such therapy may increase right atrial pressure (Fletcher *et al*., 2012). Since coronary and cerebral perfusion pressures are defined by the gradient between aortic and right atrial pressure, a disproportionate increase in right atrial pressure will compromise cerebral and cardiac blood flow. In

Drug	Indications	Dosage	Action
Atipamezole	Alpha-2 adrenoceptor agonist overdose	0.1 mg/kg i.v., i.o.	Alpha-2 adrenoceptor antagonist
Calcium gluconate (10%)	Hyperkalaemia; hypocalcaemia; calcium channel blocker toxicity; hypermagnesaemia	0.5–1.0 ml/kg i.v.	Positive inotrope; affects cardiac threshold potential to normalize cardiac conduction
Flumazenil	Benzodiazepine overdose	0.01–0.02 mg/kg i.v., i.o.	Benzodiazepine antagonist
Magnesium sulphate	Unresponsive ventricular arrhythmia (torsade de pointes); chemical defibrillator; severe hypotension	30 mg/kg i.v.	Electrolyte chemical defibrillator
Naloxone	Narcotic overdose	0.04 mg/kg i.v., i.o.	Opioid antagonist
Sodium bicarbonate	Severe metabolic acidosis, prolonged cardiopulmonary arrest	0.5–1.0 mmol/kg i.v.	Alkalinizing agent
Isotonic crystalloid fluids	Hypovolaemia	10–20 ml/kg bolus i.v., i.o.; repeat as needed	Increase of intravascular blood volume

20.12 Drugs administered during cardiopulmonary resuscitation for special circumstances.

animals with documented or presumed hypovolaemia, however, administration of intravenous fluids at shock rates (i.e. >20 ml/kg boluses of an isotonic crystalloid i.v., i.o.) is reasonable as it may increase venous return to the heart and intrathoracic vessels and thereby increase the efficacy of chest compressions.

Alkalinizing agents

With prolonged CPR (i.e. >10 minutes), administration of sodium bicarbonate (1 mmol/kg, diluted i.v.) may be considered (see Figure 20.12). Under these circumstances, the associated metabolic acidosis can be profound and critically impair cellular and subcellular processes. However, the acidosis will quickly resolve after ROSC is established, and excessive intra-arrest sodium bicarbonate administration could then lead to marked metabolic alkalosis. Thus, the administration of sodium bicarbonate should be limited to one dose, unless a continued metabolic acidaemia with a pH of less than 7.1 is found by acid–base analysis of a venous blood sample or hyperkalaemia is considered a cause of CPA.

Corticosteroids

The benefit of corticosteroid administration during CPR has not been demonstrated in experimental or clinical studies. On the other hand, negative effects of corticosteroids on gastrointestinal tract and renal blood flow are well established. Hence, the resulting unfavourable risk:benefit ratio has led to the recommendation not to use corticosteroids routinely during CPR.

Other drugs

Administration of additional drugs may be considered on a case-by-case basis in relation to specific electrolyte or metabolic abnormalities, or with certain toxicities (see Figure 20.12). Calcium gluconate (50 mg/kg i.v., i.o.) should be given if hypocalcaemia, calcium channel blocker toxicosis or hyperkalaemia are considered causative elements of the CPA. However, calcium should not be routinely administered, as evidence for a general benefit is lacking and injury may be associated with hypercalcaemic reperfusion. If beta-blocker or calcium channel blocker toxicity is identified as the cause of CPA, glucagon (0.1 mg/kg i.v.) administration should be considered. In the presence of severe hypoglycaemia, glucose (0.5 g/kg i.v.) should be administered.

Electrical defibrillation

Electrical defibrillation remains the method of choice for the conversion of pulseless VT or VF to sinus rhythm (see Figure 20.4). As previously stated, VF is much less common in dogs and cats than in humans, and so the overall need for defibrillation is significantly less.

There are two main types of defibrillators: monophasic and biphasic. Monophasic defibrillators emit a single waveform from one paddle to the other, whereas biphasic defibrillators have current that flows from one paddle to the other and then back again. Numerous studies have demonstrated that biphasic defibrillation is more effective at achieving ROSC with less energy in both humans and dogs (Rozanski *et al*., 2012). In addition, biphasic defibrillation is more likely to result in VF conversion after a single countershock, as opposed to the previously recommended series of three. This has the benefit of allowing for more prompt resumption of chest compression. Given these benefits, all defibrillators currently being made are biphasic. In dogs and cats, the defibrillator energy chosen is 2–4 J/kg for biphasic and 4–6 J/kg for monophasic external defibrillation.

Electrical defibrillation should be performed as soon as VF is diagnosed and equipment has been prepared to execute the first shock. In sequence, VF will be diagnosed during the 3–5 second chest-compression pause between two 2 minute BLS cycles, followed by immediate resumption of chest compressions. Chest compressions are then interrupted once more for a time just long enough to deliver that shock, but are immediately resumed thereafter with success of the defibrillation not being assessed until the next scheduled interruption for rhythm analysis 2 minutes later. This approach will lead to minimum interruptions in chest compressions, maximum myocardial blood flow, and therefore increased likelihood of successful defibrillation.

Along with the timing, good defibrillation technique is important. In order to achieve the most effective defibrillation, the electrical current should be transmitted directly across the heart. To facilitate this in closed-chest defibrillation, the patient should be placed in dorsal recumbency, allowing placement of the paddles on either side of the chest, avoiding contact between the paddles and the table (Figure 20.13a). Alternatively, some defibrillators allow the use of a flat paddle that can be placed under the patient in lateral recumbency (Figure 20.13b). The latter set-up will greatly reduce the amount of time needed for the shock delivery and hence will minimize the interruption in chest compressions to a few seconds. Ideally, the hair should be clipped on both sides of the chest, although the urgency of the situation may preclude this in all animals other than



20.13 (a) Defibrillator paddle position in dorsal recumbency. (b) Anterior–posterior paddle assembly. A flat paddle can be placed underneath the patient, allowing defibrillation in lateral recumbency.

those with an extremely long or dense hair coat. A liberal amount of high-conductivity gel is applied to both paddles to ensure adequate contact. Prior to discharging the defibrillator, the operator should announce 'Clear' and make sure that no one is in contact with the patient or the table, to avoid inadvertent shock to personnel.

After defibrillation, cardiac compressions should be immediately resumed for another 2 minute BLS cycle. If VF is still present at the next ECG analysis, dose escalation by 50% should be considered once for the subsequent defibrillation. In addition, adrenaline (0.01 mg/kg i.v., i.o.) should be administered. If repeated attempts to defibrillate continue to be unsuccessful, it may be beneficial to administer a dose of amiodarone or lidocaine as previously described.

Open-chest CPR

OC-CPR is associated with improved cardiac output and increased incidence of ROSC. However, this procedure involves the need for rapid thoracotomy and associated increases in cost, resource requirement and post-resuscitation morbidity. As such, OC-CPR is not routinely used and the clinical circumstances in which OC-CPR is absolutely indicated are few. Circumstances in which closed-chest CPR is likely to be less effective, or potentially harmful, include severe chest trauma, fractured ribs, pneumothorax, haemothorax, pericardial effusion, diaphragmatic hernia and other primary thoracic diseases (neoplasms, foreign bodies). In addition, cardiac output generated by the thoracic pump mechanism is thought to decrease significantly in very large canine patients (35–40 kg) and those with flat chest conformation (e.g. English Bulldogs). Some might consider failure to achieve ROSC with closed-chest CPR to be grounds for OC-CPR. However, prolonged duration of ineffective CPR may negate any beneficial effect of OC-CPR if it is employed too late. Given that functional and structural brain injury in dogs has been shown to occur after untreated CPA of 6–8 minutes, a decision for OC-CPR has to be timely, in order to take full advantage of the increased efficacy of this technique. Further, it would generally be considered contraindicated to perform OC-CPR in patients known to have a coagulopathy.

Once the decision is made to perform OC-CPR, external chest compressions should be performed until the necessary equipment is available. To limit contamination, the hair should be clipped and antiseptic solution applied to the skin prior to making the approach.

The chest is opened by making a vertical, intercostal incision from the top of the scapula to approximately 4 cm from the sternum on the left thoracic wall, at the cranial aspect of the 6th rib (5th intercostal space), avoiding the intercostal vessels and nerves. Care must be taken not to damage the lung when entering the thoracic cavity. Once the chest is entered, the 5th and 6th ribs are spread apart and the lungs are reflected dorsally and caudally. The pericardium is grasped and opened near the apex of the heart, and reflected dorsally, exposing the ventricles. In smaller patients, the heart is grasped between the thumb and forefinger and direct cardiac massage is initiated at a rate of approximately 100 compressions per minute. In larger patients, the heart is held between the palm and fingers, using a reverse-milking motion to compress the heart. Excessive force during direct cardiac compression should be avoided as it can result in severe cardiac trauma, cardiac dysrhythmias and VF.

The colour, tone and rhythm of the heart can be evaluated once the chest is open. The presence of adequate ventricular filling can be assessed, and a decision made whether additional fluid resuscitation is required. In larger dogs, the aorta can be compressed dorsally against the spine with the thumb of the opposite hand, which promotes preferential blood flow to the heart and brain.

Should OC-CPR prove to be successful in establishing ROSC, the thorax should quickly be explored for overt sources of bleeding, and lavage performed to remove any gross contamination. The thoracotomy site itself will need to be closed with placement of a thoracostomy tube. Specific techniques are beyond the scope of this chapter and the reader is referred to relevant surgical texts (e.g. *BSAVA Manual of Canine and Feline Head, Neck and Thoracic Surgery*).

When to discontinue advanced life support

The decision to discontinue ALS is dependent on a number of factors defined by futility considerations and the owner's wishes. Decision-making on grounds of CPR duration alone is not recommended as many, albeit anecdotal, reports indicate that successful resuscitation is possible even after prolonged (e.g. 60 minutes) CPR. A major consideration is the underlying cause for CPA. For patients experiencing an anaesthetic arrest, or for other potentially reversible causes of CPA, it is reasonable to continue efforts for an extended period of time (perhaps 30–40 minutes or more) as the patient may have been previously healthy and/or may have a better prognosis for meaningful long-term survival. In contrast, patients that have arrested due to severe systemic illness, or that have irreversible comorbidities that severely impair their quality of life, already have a guarded prognosis and will have all the sequelae associated with CPA superimposed on their primary disease process, making continuation of CPR beyond 10–15 minutes much less meaningful, and supporting an earlier discontinuation of ALS.

Another potential consideration is the cost associated with CPR and PCA care. A longer period of CPA, even if supported by CPR, is likely to be associated with more significant complications and a greater intensity and cost of care should ROSC be achieved. For clients with financial constraints, prolonged heroic efforts seem ill-advised. Next to economic thoughts, the owner's beliefs and wishes may also impact the duration of CPR. Owners may ask for continued efforts even if they are considered futile, or if they are en route and want to be present to say good-bye while their pet is still 'alive'. Under these circumstances it is up to the individual clinician to find a balance between the client's wishes and what is medically/ethically reasonable to do, not to mention the potential toll that fruitless CPR efforts can have on the patient care team.

Post-cardiac arrest care

Once ROSC has been observed, the initial goal for the first few minutes of PCA care is to prevent reoccurrence of CPA. PCA care then aims towards reversing or attenuating the pathophysiological processes typical of the post-resuscitation phase: ischaemia-reperfusion injury, anoxic brain injury, post-arrest myocardial dysfunction and, maybe of most importance in veterinary medicine, ongoing precipitating pathology.

Preventing re-arrest during early ROSC

As the majority of animals that are initially successfully resuscitated experience another arrest within a few hours of ROSC, the first goal of PCA care is to aggressively support circulation and perfusion of vital organs (e.g. brain and myocardium), thereby reducing further injury to these tissues and preventing re-arrest. Common monitoring modalities, such as pulse oximetry or Doppler sphygmomanometry, will resume functioning again with ROSC and can aid the clinician in closely and continuously assessing the cardiovascular and respiratory status of the patient. Identification of significant abnormalities in electrolytes, glucose, acid–base status, haematocrit, arterial oxygenation and ventilation early after ROSC is an initial priority, including the correction of reversible causes of cardiac arrest (see Figure 20.1). Hypoxaemia, severe anaemia, hypotension, hyperkalaemia or hypocalcaemia require rapid correction.

Frequencies of different re-arrest rhythms have not been determined in veterinary medicine, but in humans, shockable (VF/pulseless VT) and non-shockable (PEA and asystole) rhythms are equally prevalent. VT is common after ROSC. If it persists, administration of lidocaine (2 mg/kg i.v. slow bolus, followed by a 30–50 μg/kg/min i.v. infusion) should be considered. Vasopressor administration is commonly required to support vascular tone and treat hypotension. Post-ischaemic left ventricular systolic dysfunction can be attenuated with infusion of positive inotropes such as dobutamine. As adrenaline is effective in increasing both vascular tone via alpha-1 adrenoceptors and cardiac contractility via beta-1 adrenoceptors, a constant rate infusion (CRI) of adrenaline (0.1–0.5 μg/kg/min i.v.) titrated to effect can initially be useful to correct hypotension and prevent reoccurrence of CPA.

A respiratory management strategy has been suggested by RECOVER that includes initial ventilation and oxygenation endpoints. It states that an arterial partial pressure of carbon dioxide (P_aCO_2) of 32–43 mmHg in dogs and 26–36 mmHg in cats should be targeted by assisted (either manual or mechanical) ventilation. Hence, monitoring ventilation with either $ETCO_2$ or repeat P_aCO_2 is important. As many patients with prolonged CPA will not initially resume normal ventilation, the need for temporary provision of ventilatory support is not unusual and may be essential for prevention of re-arrest. Moreover, both hypoxaemia and hyperoxaemia should be avoided by titrating oxygen supplementation to peripheral capillary oxygen saturation (S_pO_2) values of 94–98% or an arterial partial pressure of oxygen (P_aO_2) of 80–100 mmHg. After initial haemodynamic and respiratory stabilization is accomplished, care should be directed towards ongoing pathophysiological processes typical for the PCA phase, including systemic inflammation, ischaemic brain injury, myocardial dysfunction and underlying disease processes.

Post-cardiac arrest phase as a sepsis-like syndrome

ROSC after the global ischaemic event of CPA leads to a profound whole-body ischaemia–reperfusion syndrome that has been recognized as 'post-resuscitation disease'. It shares many clinical and pathological aspects with severe sepsis, including effects on inflammation, coagulation and the endothelium, and has been described as a 'sepsis-like syndrome' or systemic inflammatory response syndrome (SIRS) (Adrie *et al*., 2002).

Hence, clinical characteristics of sepsis/SIRS and multi-organ dysfunction syndrome may be expected in dogs and cats after CPA. Therapeutic considerations apart from the use of antibiotics may be similar to the care of septic patients, including early haemodynamic optimization, glycaemic control and treatment of relative adrenal insufficiency (Figure 20.14). As for any critical care patient, it is important to realize that treatment is highly individualized, carefully adjusted to a patient's needs and response to treatment. Continuous patient monitoring is therefore very important, and veterinary providers that are not equipped for continuous 24-hour care of critically ill PCA patients may consider referral to a specialized facility (Fletcher *et al*., 2012).

Drug	Indications	Dosage	Action
Adrenaline	Severe bradycardia Hypotension due to vasodilation Prevention of re-arrest early after ROSC	0.1–1.0 μg/kg/min i.v. CRI	Vasopressor and positive inotrope and chronotrope; alpha- and beta-adrenergic agonist
Dobutamine	PCA myocardial dysfunction	5–20 μg/kg/min i.v. CRI	Positive inotrope Beta-adrenergic agonist; can cause seizures in cats
Dopamine	Bradycardia Low cardiac output Hypotension	5–10 μg/kg/min i.v. CRI for increased cardiac contractility and cardiac output 10–20 μg/kg/min i.v. CRI for vasoconstriction	Noradrenaline precursor Dose-dependent Alpha- and/or beta-adrenergic agonist
Hypertonic saline, 7.0%–7.5%	Clinical signs of intracranial hypertension	3–5 ml/kg (dog) 2 ml/kg (cat) i.v., i.o., over 5–10 minutes	Reduction of cerebral oedema
Lidocaine	Ventricular tachycardia Ventricular fibrillation resistant to electrical defibrillation	Dogs: 2–4 mg/kg i.v. bolus followed by 30–80 μg/kg/min i.v. CRI Cats: 0.25–0.5 mg/kg i.v. bolus followed by 10–20 μg/kg/min i.v. CRI	Class IB ventricular antiarrhythmic
Mannitol	Clinical signs of intracranial hypertension Oliguria	0.5–1.0 g/kg i.v. given slowly over 10 minutes	Osmotic diuretic; reduction of cerebral oedema
Noradrenaline	PCA hypotension due to vasodilation	0.05–0.5 μg/kg/min i.v. CRI	Vasopressor; preferential alpha-1 adrenoceptor agonist
Vasopressin	PCA refractory hypotension due to vasodilation	0.5–5.0 mU/kg/min	Vasopressor; may be more effective in severe acidosis

20.14 Drugs administered for post-cardiac arrest (PCA) care. CRI = constant rate infusion.

Haemodynamic optimization

Early goal-directed therapy (EGDT) was shown to be a successful strategy for haemodynamic optimization in humans with severe sepsis and septic shock more than a decade ago (Rivers *et al*., 2001). EGDT describes an algorithmic approach to resuscitation with predefined resuscitation endpoints. While the benefit of EGDT as described by Rivers *et al*. (2001) has recently been challenged, the concept of EGDT has found wide clinical application and elements of it are now part of usual clinical care in human medicine (Kalil *et al*., 2017; Rhodes *et al*., 2017). A modified EGDT approach has been implemented in humans for PCA care as an early haemodynamic optimization protocol, but the exact haemodynamic goals remain uncertain and may be influenced by the specific patient condition (Gaieski *et al*., 2009; Callaway *et al*., 2015). RECOVER suggests a veterinary PCA haemodynamic optimization algorithm (Fletcher *et al*., 2012) with resuscitation endpoints being:

- Central venous pressure (CVP): 0–10 cmH_2O
- Mean arterial blood pressure (MAP): 80–120 mmHg
- Perfusion parameters: central venous oxygen saturation ($S_{cv}O_2$) >70%; lactate <2.5 mmol/l.

These should be combined with physical examination endpoints, such as pink mucous membrane colour, capillary refill time of <2 seconds, normal pulse quality and production of urine. Electrocardiography with treatment of tachycardia or bradycardia and significant arrhythmias, combined with echocardiographic assessment of left ventricular function, may also be included. This algorithmic, individualized and closely monitored approach will permit aggressive yet safe fluid, inotropic and pressor therapy titrated to an individual patient's needs. It is important to recognize once more that the variability in PCA patient response to injury and treatment is considerable and does not permit a 'one-size-fits-all' therapeutic approach.

Glycaemic control

PCA hyperglycaemia commonly occurs in humans, and evidence suggests it has a positive association with worse neurological outcome and mortality. Experimental studies in dogs replicate these findings and suggest that ischaemic brain injury is exacerbated by hyperglycaemia. Studies in humans showed that insulin infusions to achieve tight glycaemic control (4.4–6.1 mmol/l) after ROSC may lead to frequent iatrogenic hypoglycaemia. Since evidence of a benefit of such tight glycaemic control over a more moderate target of less than 10 mmol/l is lacking, the latter is currently recommended in human PCA care. In dogs and cats after cardiac arrest a similar moderate glucose control target may be considered. Administration of intravenous insulin for glycaemic control follows the recommendations for sepsis.

Critical illness-related corticosteroid insufficiency

Steroids are essential to the physiological response to severe stress and are important for regulation of vascular tone and endothelial permeability. Critical illness-related corticosteroid insufficiency (CIRCI), formerly known as relative adrenal insufficiency (RAI), during the PCA phase was demonstrated in numerous human studies and was shown to be associated with a worse outcome. Steroid administration, even at a low dose, remains a matter of debate in septic shock despite much research, and has not been sufficiently studied in PCA patients to make firm recommendations. Due to the well defined risks of glucocorticosteroid administration (including infection, peptic ulcer and worsening of post-ischaemic neurological injury), routine administration of corticosteroids during PCA care in dogs and cats is not recommended (Fletcher *et al*., 2012). In fluid-resuscitated animals with refractory hypotension or vasopressor-dependent shock after CPA, with or without documented CIRCI, administration of low-dose hydrocortisone (1 mg/kg i.v. followed by either 1 mg/kg i.v. q6h or an intravenous infusion of 0.15 mg/kg/h) may be considered (Fletcher *et al*., 2012).

Anoxic brain injury

In humans, cerebral dysfunction after CPA is of great importance and constitutes the primary cause of death. In small animals, PCA brain injury after experimental and clinical CPA has been described, although sufficient epidemiological data to determine its relative importance are currently lacking. PCA brain injury is a consequence of the combined effect of global cerebral ischaemia and subsequent reperfusion; the current working hypothesis suggests that much of the injury sustained occurs during reperfusion and not ischaemia. This is of therapeutic significance, as the clinician will be able to influence the reperfusion process to a larger extent than the actual cardiac arrest or ischaemia.

Titrated oxygenation

Elaboration of reactive oxygen species (ROS) plays a significant role in the pathophysiology of the PCA syndrome. Highly reactive ROS will lead to cell membrane damage, lipid peroxidation, DNA damage and protein alterations, and lead to cell apoptosis and necrosis (Neumar, 2011). Reduction of oxidative injury, such as by titration of inspired oxygen concentration (F_iO_2), is an important therapeutic strategy of PCA care.

In dogs, limitation of F_iO_2 during the first 60 minutes of reperfusion not only led to improved functional and morphological outcomes, but also limited ROS generation (Liu *et al*., 1998; Balan *et al*., 2006). On the other hand, rapid reoxygenation after CPA is the central goal of CPR. This absolute requirement to reintroduce oxygen collides with the toxic potential of oxygen as the substrate for ROS. Both hyperoxaemia and hypoxaemia can increase neurological injury and thus, a titrated approach to avoid either condition should be used. In fact, in dogs with ROSC after experimental CPA, titration of the F_iO_2 to a target S_pO_2 of 94–96% compared with maximum oxygen administration (F_iO_2 = 1.0) attenuated neuronal degeneration in vulnerable brain regions, and led to improved neurological outcomes (Balan *et al*., 2006). The current RECOVER guidelines recommend that oxygen administration should be titrated to the minimum amount required to maintain normoxaemia (P_aO_2 = 80–100 mmHg or S_pO_2 = 94–98%), thereby avoiding both hypoxaemia and hyperoxaemia (Fletcher *et al*., 2012).

Seizure prophylaxis and treatment

Seizures can occur in dogs and cats (and in humans) after successful resuscitation from CPA. In humans, seizures during the first 72 hours after ROSC indicate a worse neurological outcome. In addition, seizures can occur with no associated motor signs present. In humans that remain comatose after CPA, the non-convulsive status epilepticus can only be, and frequently is, identified with

electroencephalography. Harm can be caused by seizure activity as it leads to an unfavourable tissue oxygen demand:supply ratio. Hence, monitoring for seizures has to be a priority, and seizures need to be aggressively treated with benzodiazepines (e.g. diazepam at 0.5 mg/kg i.v.), barbiturates (e.g. phenobarbital at 16 mg/kg i.v. divided into four doses (i.e. 4 mg/kg i.v. q6h)) or other drugs such as levetiracetam if necessary. The RECOVER initiative, based on limited evidence, further recommends that prophylactic administration of barbiturates may be considered, especially in animals that remain comatose after ROSC (Fletcher *et al*., 2012).

Hyperosmotic therapy

In humans, cerebral oedema has been described after CPA and was associated with unfavourable neurological outcomes. Cerebral oedema severe enough to cause intracranial hypertension after CPA in humans is infrequent, but may compromise cerebral blood flow. In one experimental canine study, administration of hypertonic fluids was effective in reducing cerebral oedema after reperfusion from prolonged cerebral anoxia. However, neither survival nor neurological functional outcome was affected. In the absence of any strong evidence for or against the routine use of hyperosmotic agents after CPA in any species, the RECOVER initiative suggests that the use of mannitol (0.5–1.0 g/kg i.v.) or hypertonic saline (7.2% NaCl at a dose of 4 ml/kg i.v. (dogs) or 2 ml/kg i.v. (cats) administered over 5–10 minutes) can be considered if the presence of cerebral oedema is supported by clinical signs (e.g. coma, stupor or decerebrate posture) (Fletcher *et al*., 2012). Unfortunately, differentiating these clinical signs from PCA brain injury unrelated to cerebral oedema or from effects of sedatives will not always be easy. If mannitol is administered, its effect on diuresis and electrolyte balance needs to be taken into consideration and fluid supplementation adjusted accordingly.

Optimization of cerebral blood flow

Experimental data suggest that there is an impediment to cerebral blood flow after prolonged cardiac arrest, leading to heterogeneous cerebral blood flow distribution with areas of no blood flow next to areas of hyperaemia. In dogs, increasing mean arterial blood pressure to supranormal levels (e.g. 120 mmHg) was effective in increasing flow to hypoperfused brain regions, thereby abolishing this heterogeneity. The RECOVER initiative therefore recommends targeting an increased blood pressure (MAP = 120–140 mm Hg) during the first 4 hours of reperfusion after prolonged CPA associated with severe neurological injury (e.g. coma). A more physiological target may be reasonable when ROSC was achieved after only a short period of CPA with mild to moderate neurological injury. In any case, a low arterial blood pressure may be harmful and should be aggressively treated with fluid administration, positive inotropes and/or vasopressors according to the clinical situation (see Chapters 3 and 4).

Ventilation can also influence cerebral blood flow. Post-ROSC hyperventilation (i.e. decreased P_aCO_2) may cause cerebral arterial constriction and reduce cerebral blood flow. It is important strictly to avoid low P_aCO_2 values during the PCA phase and to monitor and regulate ventilatory function. The RECOVER guidelines recommend a target P_aCO_2 of 32–43 mmHg in dogs and 26–36 mmHg in cats, in line with the normal values for these species (Fletcher *et al*., 2012).

Temperature management during the PCA phase

Targeted temperature management (TTM), formerly referred to as mild therapeutic hypothermia (MTH), describes the therapeutic control of the core body temperature in the range of 32–36°C (Brodeur *et al*., 2017). In conditions of ischaemia and reperfusion injury, hypothermia has been shown to exert a neuroprotective effect via many pathways, including mitochondrial protection, decrease in cerebral metabolism, impediment of calcium inflow into cells, reduction of neuronal excitotoxicity, reduced elaboration of ROS, attenuated apoptosis and control of seizure activity (Polderman, 2009).

TTM has been proven to be effective in humans with out-of-hospital cardiac arrest that remain comatose after ROSC, while conclusive evidence for patients after in-hospital cardiac arrest is currently lacking. No clinical data are currently available to prove the benefit of TTM in dogs or cats; however, evidence suggests that the benefit of cooling extends beyond species borders. In addition, the risk associated with the use of TTM is low. Hence, the RECOVER initiative recommends administering TTM in dogs and cats that remain comatose after ROSC (Fletcher *et al*., 2012). Cooling blankets, surface application of ice-packs or bags, intravenous infusion of ice-cold saline, or more advanced tools such as endovascular cooling devices can be used to achieve and maintain TTM. Early cooling is more effective than delayed cooling. Based on best evidence TTM for 24–48 hours is currently recommended. Fast rewarming and hyperthermia are harmful and rewarming at a slow rate of 0.25–0.5°C per hour is recommended.

Depending on the temperature target chosen, side effects of cooling may include an increased muscle tone and shivering, and increasing oxygen consumption, metabolic rate, and respiratory and heart rates. Sedation to prevent these consequences is therefore essential, but may lead to the need for intubation and mechanical ventilation. The clinical management of these cases may be time-consuming and costly and is comparable with mechanically ventilated patients. Other adverse effects include disturbances in metabolism, acid–base status, electrolytes, ECG, drug elimination, coagulation and immune function. However, adverse effects during TTM in humans are limited, and do not impact on mortality in clinical studies. Notwithstanding, the side effect profile may be different in small animals. If pre-existing disease processes, such as sepsis or coagulopathies, are present the benefit of TTM should be carefully weighed against the risk.

Dogs and cats are often spontaneously hypothermic after ROSC. Allowing a PCA patient to remain hypothermic (permissive hypothermia) and to slowly rewarm may be an alternative to induced TTM, while at the same time eliminating the harm associated with fast rewarming. It is reasonable to target a rewarming rate of no more than 0.5°C per hour (Fletcher *et al*., 2012). Moreover, fever or hyperthermia should be prevented.

Myocardial dysfunction

PCA myocardial dysfunction (MD) has been well described in both humans and animals (Nakamura *et al*., 2012). MD causes biventricular diastolic and systolic dysfunction. Cardiac function can be further impaired by ventricular tachyarrhythmias. Diagnosis and monitoring is best accomplished by echocardiography. MD is reversible and will resolve over the first 2–3 days after ROSC. PCA

dobutamine administered as a CRI at typical clinical doses was shown to be effective to improve cardiac contractility in this condition (Vasquez *et al*., 2004). Of note, the presence of MD may increase the risk for hydrostatic pulmonary oedema and should be taken into consideration when devising a fluid therapy and monitoring plan.

Persistent precipitating pathology

Most dogs and cats that undergo CPR experience CPA in a veterinary hospital. Hence, the root cause of CPA is commonly a disease process, such as severe sepsis, trauma or respiratory failure. In dogs and cats, hypoxaemia (36%), shock (18%), anaemia (13%), arrhythmia (8%), multiple organ disfunction syndrome (6%), traumatic brain injury (5%), anaphylaxis (1%) and other causes for CPA (21%) were identified (Hofmeister *et al*., 2009). Many of these conditions will persist after ROSC and may impact the overall quality of life of the pet. Such persistent precipitating pathology will not only impact the specific PCA care required but will also influence the prognosis presented to the pet owner and the decision for euthanasia. Data from human clinical studies also confirms that pre-arrest factors such as neurological function, presence of mechanical ventilation, renal and hepatic insufficiency, sepsis, malignancy and hypotension are independently associated with a lower likelihood of survival (Chan *et al*., 2012). The absence of severe pre-existing disease in a large proportion of patients with anaesthetic CPA may be one reason for the comparatively high survival-to-discharge rate in this population.

Considering the many factors involved, the PCA patient will be part of an incredibly diverse population, and critical care principles need to be applied according to the overall disease picture with specific attention given to optimize oxygenation, ventilation, circulation and metabolism. The overarching goal is to allow the animal to fully realize its potential for a meaningful outcome while protecting its dignity.

Prognostication

There is currently little veterinary evidence available that would inform the clinician on objective prognostication in patients after ROSC. Clinical experience suggests that when complete brain ischaemia lasts longer than 5 minutes or the cardiac resuscitative effort lasts in excess of 20 minutes, neurological recovery may be unsatisfactory and long-term survival reduced. Anecdotal information suggests that survival to discharge in dogs has been possible after as long as 60 minutes of CPR. Hence, duration of CPR cannot be utilized as the only decision- making tool. Age, concurrent disease and current medical or surgical complications are all important factors in determining outcome. Rapid recovery of eyelid, pupillary and swallowing reflexes, resumption of a normal arterial pulse and breathing pattern, improving level of consciousness and the maintenance of normal body temperature are considered good prognostic signs. Most dogs and cats that show signs of recovery within 5–10 minutes of ROSC will recover with normal brain function. Neurological assessment may, however, be confounded by residual effects of drugs administered during CPR, sedatives, anaesthetics and hypothermia.

In principle, progressive mental deterioration, seizures or unconsciousness, particularly after initial partial recovery, dilated fixed pupils, loss of eyelid and swallowing reflexes, prolonged respiratory arrest and gradual decreases in body temperature are poor prognostic signs. Of note, findings in human studies show that it is difficult to reliably predict a negative neurological outcome with high certainty before 24–72 hours after ROSC, and it is therefore reasonable to observe progression of neurological abnormality for some time, if haemodynamic and respiratory status allow.

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Chapter 21

Anaesthesia, sedation and analgesia of the critical patient

Giacomo Gianotti and Paulo Steagall

Critically ill patients routinely require either anaesthesia or sedation in order to facilitate diagnosis or treatment. Many drugs are discussed in this chapter and their availability and licensing will be different in different jurisdictions around the world. Clinicians should familiarize themselves with the local regulatory framework and ensure they abide by it; for example, in the UK, the prescribing cascade should be followed, with specific informed consent obtained from the owners if drugs are to be used off licence.

Sedation

Sedatives are commonly used in critical patients to provide patient comfort, reduce stress response and facilitate procedures. Common situations that require the administration of sedatives include:

- Rendering the patient cooperative during non-invasive diagnostic procedures or treatments such as performing a physical examination, obtaining vascular access, catheter placement or bandage changes
- Decreasing opioid-induced dysphoria, especially in the immediate postoperative period
- Controlling restless pacing or barking that arises from hospitalization anxiety.

The use of sedation has potential risks that most commonly arise from the impact of sedative drugs on the cardiovascular and respiratory systems. This is especially true for the critically ill patient, in which these systems may already be severely compromised and deprived of their reserves by underlying medical conditions. For this reason it is of critical importance to perform a detailed assessment of the patient prior to the administration of sedative or anaesthetic drugs. A thorough physical examination will help the clinician to select the appropriate sedative, analgesic and anaesthetic protocols tailored to the individual.

There is a common misconception that sedation is safer than general anaesthesia (GA). However, in many circumstances GA may be safer since it allows rapid control of the airways, minimizing the risk of regurgitation, aspiration of foreign material and upper airway obstruction, while giving the opportunity to more effectively supplement oxygen and precisely control ventilation. An anaesthetized patient is normally closely monitored with appropriate equipment, which increases the ability to intervene promptly in case of an adverse event. Although invasive monitoring may not be possible in a sedated patient, it is recommended that these patients receive a similar level of monitoring to those under GA, with recording of vital signs as a minimum on a regular basis.

Drugs commonly used for sedation

Phenothiazines

The most commonly used phenothiazine in veterinary medicine is acepromazine. This drug is classified as a tranquillizer with neuroleptic effects. Acepromazine has anti-dopaminergic effects that account for its sedative effects; however, it also blocks vascular alpha-adrenergic type 1 receptors. For this reason, acepromazine has the potential to cause hypotension and should be used with caution in patients whose cardiovascular system is compromised (hypotension, hypovolaemia). Dogs become less responsive to dopamine for treatment of hypotension after acepromazine administration (Sinclair and Dyson, 2012). Other non-sedative effects include antiemetic, antihistaminic and anti-arrhythmogenic properties.

Acepromazine has a long duration of action (4–6 hours), without the benefit of reversibility. The drug has extensive hepatic metabolism and renal excretion of inactive metabolites. It should be used with caution in patients with liver disease due to potential prolonged duration of action.

Historically, the drug has been contraindicated in dogs with a history of seizures because of the presumed potential to reduce the seizure threshold, but more recent literature provides evidence that acepromazine may be used in patients suffering from epilepsy (Tobias *et al.*, 2006; McConnell *et al.*, 2007). This is particularly true when anxiety is the triggering cause of seizures (Figure 21.1).

Acepromazine uses	Dose	Comment
Sedation	0.005–0.01 mg/kg i.v. 0.01–0.05 mg/kg i.m.	• Anxiolytic • Tranquillizer for dogs with upper airway obstruction • Attenuation of dysphoria from opioids
Neuroleptic analgesia	0.01–0.05 mg/kg i.m. + butorphanol, methadone or morphine	• Premedication • Potential for hypotension

21.1 Commonly used doses of acepromazine in the dog and cat.

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Benzodiazepines

Diazepam and midazolam are commonly used, and are classified as sedatives with anxiolytic properties. These drugs are administered for sedation and as adjuncts to GA, due to their reversibility by flumazenil and wide margin of safety, especially with regard to the cardiovascular and respiratory systems. Midazolam is well absorbed after intramuscular and intranasal administration, has a favourable pharmacokinetic profile with rapid clearance without production of active metabolites, and does not have propylene glycol as part of its formulation, which may produce pain on injection and cardiovascular depression at high and repeated doses. For these reasons midazolam is preferred to diazepam for prolonged infusions or administration by routes other than intravenous. Both drugs are extensively metabolized by the liver, so care must be taken when using them in patients with hepatic insufficiency or hepatic encephalopathy. These drugs are considered respiratory sparing if used alone; however, they can contribute to hypoventilation if combined with other respiratory depressants (i.e. opioids or inhalational anaesthetics) (Figure 21.2).

Diazepam/midazolam doses	Comments
Premedication: 0.1–0.5 mg/kg i.v., i.m.	• Use in combination with an opioid • Can cause excitement, especially in cats • Diazepam should only be given i.v.
Seizures: loading dose 0.2–0.5 mg/kg ± CRI at 0.1–0.5 mg/kg/h i.v.	• Midazolam is better suited to repeated administration (less accumulation and no propylene glycol)
Co-induction of anaesthesia: 0.1–0.2 mg/kg i.v.	• To decrease the dose of induction drugs and as muscle relaxant when ketamine is used • Evidence suggests that midazolam causes some degree of vasodilation but diazepam does not
Mechanically ventilated patients: loading dose 0.1–0.2 mg/kg i.v. + CRI at 0.1–0.3 mg/kg/h i.v.	• To decrease the dose of anaesthetic drugs and improve thoracic compliance

21.2 Commonly used doses of benzodiazepines in the dog and cat. CRI = constant rate infusion.

Alpha-2 adrenergic receptor agonists

Medetomidine and dexmedetomidine are commonly used alpha-2 adrenergic receptor agonists. Although effective sedatives, they dramatically impact cardiovascular function via activation of peripheral and central alpha-adrenergic receptors. These effects become significant in critically ill patients especially, if cardiovascular instability is already present. Hypertension and reflex bradycardia are commonly observed, which lead to decreases in cardiac output and coronary perfusion, a significant increase in cardiac work, and a decrease in tissue oxygen delivery. Although the cardiovascular side effects dramatically limit the use of these drugs in critically ill patients, they are very effective sedatives, especially in aggressive animals, and good analgesics, and can be fully reversed with the competitive antagonist atipamezole. Doses higher than 0.5–1 μg/kg intravenously are unlikely to be needed in critically ill patients even though these drugs may be licensed at higher doses.

Alpha-adrenergic receptors are ubiquitous throughout the body and have relevant effects on various organ systems, including decreased gastrointestinal secretions and motility, decreased stress response to tissue trauma, hyperglycaemia, vomiting, hypothermia, increased urine production, and decreased intraocular and intracranial pressure (ICP) (Sinclair, 2003) (Figure 21.3).

Medetomidine doses[a]	Comments
Premedication: 1–10 μg/kg i.m.; 0.5–2.0 μg/kg i.v. (slow)	• Medetomidine is the racemic mixture of levomedetomidine and dexmedetomidine
Sedation/analgesia: loading dose 0.5–1.0 μg/kg + CRI at 0.5–2.0 μg/kg/h i.v.	• To decrease adverse cardiovascular effects, dilute the loading dose in 5–10 ml of saline and give slowly i.v. over 10 minutes • If used in combination with an opioid, hypoventilation may occur, therefore monitor closely and provide oxygen
Adjunct in the management of seizures: loading dose 0.5 μg/kg + CRI at 0.5 μg/kg/h i.v.	• To facilitate sleep and decrease anxiety in patients receiving continuous i.v. treatments for seizures
Atipamezole reversal	**Comments**
10 times the dose of dexmedetomidine and 5 times the dose of medetomidine	• With commonly used preparations this equates to the same dose in volume as that of medetomidine and dexmedetomidine. The label use is only i.m. • Atipamezole will lead to the opposite effects of the agonist if given when the alpha-2 agonist is not on board (excitement, hypotension and tachycardia)

21.3 Commonly used doses of alpha-2 agonists in the dog and cat. CRI = constant rate infusion. [a]Doses for dexmedetomidine are half that for medetomidine.

Opioids

Many opioids can safely be used for sedation, induction and maintenance of anaesthesia. They provide profound analgesia (acting as mu (μ) agonists) with some degree of hypnosis, but have minimal effects on the cardiovascular system, maintaining unaltered myocardial contractility and with marginal effects on systemic vascular resistance (Machado *et al.*, 2005). Opioid vagal-induced bradycardia and bradyarrhythmias may occur but are easily treated with anticholinergics such as glycopyrrolate or atropine.

On the other hand, opioids may cause dose-dependent respiratory depression, which becomes more relevant when they are used in combination with potent hypnotic drugs (propofol, inhalational anaesthetics) and/or in ill patients. For this reason ventilation and oxygenation should be carefully monitored, and oxygen supplementation might be required during sedation and/or mechanical ventilation needed during GA. However, depriving patients of analgesic drugs because of the potential for respiratory depression is not an appropriate ethical and medical approach (Simon and Steagall, 2017). Opioids should be used with caution in patients with increased ICP because of the potential for hypoventilation, which may have adverse effects on their neurological status. Care must be taken when using opioids in patients with arrhythmias that may be exacerbated by increases in vagal tone (third-degree atrioventricular block, sick sinus syndrome and atrial standstill) because these drugs may suppress the ventricular escape rhythm and cause cardiac arrest.

Opioids may be reversed with the competitive antagonist naloxone, keeping in mind that the analgesic effects will be also reversed. The duration of action of naloxone (~1 hour) may be shorter than that of the agonist opioid, thus the potential for re-narcotization exists (Figure 21.4).

Opioid	Dose and duration	Comments
Morphine	0.1–0.3 mg/kg i.m. q3–4 hours	• Pure agonist • Causes emesis and relevant histamine release if given i.v. • Cat: commonly causes dysphoria
Methadone	0.1–0.3 mg/kg i.m. or i.v. q3–4 hours	• Pure agonist and NMDA antagonist
Fentanyl	2–4 µg/kg i.v. + CRI at 2–4 µg/kg/h (analgesia/sedation) 5–10 µg/kg i.v. + CRI at 0.1–0.7 µg/kg/min (anaesthesia) 20 minutes (single bolus)	• Pure agonist • Short duration but potential for accumulation at higher CRI doses • Reduces the need for induction and maintenance drugs during anaesthesia by 40–50%
Butorphanol	0.2–0.5 mg/kg i.v. or i.m. ± CRI at 0.1–0.2 mg/kg/h (sedation) 0.05 mg/kg i.v. (reversal of opioid-induced dysphoria) q1 hour	• Agonist–antagonist, minimal analgesia, good sedation, antitussive • Minimal respiratory depression

21.4 Commonly used doses of opioids for sedation in the dog and cat. CRI = constant rate infusion; NMDA = *N*-methyl-D-aspartate.

Trazodone

Trazodone (2–5 mg/kg orally q8–24h, dogs and cats) is a serotonin receptor antagonist with anxiolytic, mild sedative and antidepressant properties. The drug is also a serotonin reuptake inhibitor. Recently, trazodone has been successfully administered to control anxiety in the intensive care unit (ICU) setting without adverse effects such as cardiovascular or respiratory depression. It has been also used in cats to facilitate transport into the veterinary clinic. In the critical patient it may be used in combination with opioids and benzodiazepines, without adverse effects. It is recommended to start with lower doses and then titrate the dose to effect in order to minimize gastrointestinal side effects (gagging, vomiting, colitis). Since it interferes with central serotonin receptors it should not be used in patients that are receiving other serotonergic agents. The oral formulation is the only option currently available in North America, which limits its use to animals that can safely and reliably receive oral medication (Gruen and Sherman, 2008; Jay *et al*., 2013).

General anaesthesia

Critically ill patients may require GA during the course of their hospitalization for several reasons:

- Emergency surgical procedures
- Feeding tube, central line or catheter placement
- Wound care
- Emergency control of the upper airway in animals with obstruction
- Facilitation of mechanical ventilation
- Tracheal and bronchoalveolar lavage
- Endoscopy.

Balanced anaesthesia should achieve unconsciousness, analgesia, immobility and muscle relaxation. It is important to understand that not all of these can be fulfilled with the use of a single anaesthetic agent without severely compromising the cardiovascular, respiratory and nervous systems. This is especially true for debilitated patients. For this reason different drugs and local anaesthetic techniques are combined to limit dose-dependent side effects, and to take advantage of additive and/or synergistic effects in order to obtain a suitable depth of anaesthesia (Figure 21.5).

Anaesthesia in the critically ill patient carries many challenges due to the increased risk of perioperative complications (Brodbelt *et al*., 2008). There may be limited time and information to stabilize and prepare the patient for anaesthesia. Prioritizing specific concerns while predicting and addressing perioperative complications are key to a successful outcome.

Patient assessment

Proper pre-anaesthetic assessment is of pivotal importance in the critically ill patient. A thorough history and physical examination will guide choices for essential diagnostic screening and drug selection, and allow prediction and resolution of potential concerns and complications, thus reducing morbidity and mortality. Time is normally the limiting factor when assessing and stabilizing an emergency patient, therefore special emphasis should be directed towards the cardiovascular, respiratory and central nervous systems.

Agent	Loss of consciousness	Analgesia	Muscle relaxation	Immobility	Cardiovascular depression	Respiratory depression
Inhalational anaesthetics	+++	–	+++	+++	+++	+++
Propofol	+++	–	+++	+++	++	++(+)*
Ketamine	++	++	–	++	+	+(+)*
Etomidate	+++	–	+	++	–	–
Alfaxalone	+++	–	+++	+++	++	++
Opioids	+	+++	+	+	–	+++
Benzodiazepines	+	–	+++	+	–	+
Alpha-2 agonists	++	+++	+++	++	+++	–

21.5 Pharmacological effects of drugs commonly used for general anaesthesia. + = has effect; ++ = has mild effect; +++ = has moderate effect; – = has no or minimal effect; * = the effect is dose dependent.

Cardiovascular system

Blood loss: Always optimize intravascular volume prior to GA, making sure to preserve adequate colloid oncotic pressure and oxygen-carrying capacity. Cardiovascular sparing drugs should be used (opioids, benzodiazepines, etomidate) and loco-regional anaesthetic techniques should be considered when possible to reduce anaesthetic requirements.

Arrhythmias: Depending on their nature, arrhythmias may need specific treatment (see Chapter 6). However, preoperative bradyarrhythmias (third-degree atrioventricular (AV) block, atrial standstill, sick sinus syndrome) require immediate attention because they can lead to cardiac arrest when anaesthetic drugs are administered (opioids, alpha-2 agonists, inhalant anaesthetics). In many of these cases the use of a temporary pacemaker is warranted.

Bradycardia requires treatment if associated with hypotension or second-degree Mobitz type II AV block (glycopyrrolate at 0.005–0.01 mg/kg; atropine at 0.01–0.02 mg/kg). Bradycardia and bradyarrhythmias associated with hypertension from (dex)medetomidine should not be treated with anticholinergic drugs. Instead, reversal with the alpha-2 adrenoreceptor antagonist (atipamezole) is recommended in these cases.

Bradycardia may be caused by hypothermia and electrolyte disturbances, in particular hyperkalaemia, which are non-responsive to treatment with an anticholinergic and require specific management.

Patients with ventricular tachycardia present with pulse deficits that greatly compromise tissue perfusion. Treatment for dogs includes lidocaine (2 mg/kg i.v. followed by an infusion of 50–80 μg/kg/min). Cats rarely develop ventricular tachycardia; the doses used if necessary are considerably lower than in the dog (1 mg/kg i.v. followed by 25 μg/kg/min).

Dehydration: Ideally this should be corrected prior to administering anaesthetic agents. Dehydration results in loss of free water and electrolytes, leading to haemoconcentration, circulating volume depletion and urine concentration. This will negatively impact cardiovascular function during GA, causing decreased cardiac output, arterial blood pressure and tissue perfusion. As a rule of thumb at least half of the calculated water deficit should be replaced with the same volume of a balanced electrolyte solution prior to induction of anaesthesia.

Cardiac insufficiency: In general, the goal in patients with cardiomyopathy or valvular disease is to use drugs that minimally alter cardiovascular function, combining local anaesthetic techniques with injectable and inhalant anaesthetics. Cautious use of fluid therapy is recommended since these patients may not tolerate rapid increases of intravascular volume, leading to acute cardiogenic pulmonary oedema.

Pericardial effusion: Pericardial effusion can lead to pericardial tamponade, which leads to decreased cardiac output. When relevant amounts of pericardial effusion are present, ultrasound-guided drainage prior to GA is warranted.

Respiratory system

Any patient with suspected respiratory disease should receive pre-oxygenation prior to anaesthesia. In addition, animals that are at risk of hypoxaemia produced by anaesthetic-induced cardiorespiratory depression should be pre-oxygenated.

Upper airway obstruction: Animals with brachycephalic syndrome, laryngeal paralysis, tracheal collapse or masses that occupy the oral cavity may not show clinical signs of upper airway obstruction on presentation. However, these patients may rapidly deteriorate and lose airway patency when sedated, when GA is induced, or during recovery after extubation. When sedating these patients, care must be taken to ensure that they can maintain control of their airway; the clinician must be prepared to intubate in a timely fashion if necessary. Animals with oral masses that limit direct laryngeal visualization present a unique challenge for endotracheal intubation. Titration of drugs with the goal of maintaining spontaneous ventilation while attempting to establish a patent airway is of critical importance. A variety of tracheal tube sizes, stylets and laryngoscopes should be available (see Chapter 7).

Pneumonia: Patients with pneumonia may require GA to perform a diverse spectrum of diagnostic procedures; commonly these include tracheal wash, bronchoscopy and bronchoalveolar lavage. Oxygenation and ventilation should be continuously monitored in these patients. In most cases an opioid such as butorphanol (0.2 mg/kg) can be used as premedication; anaesthesia can be induced with propofol titrated in 1 mg/kg increments to effect, and maintained with an inhalational anaesthetic (isoflurane or sevoflurane). A special T-piece can be connected between the endotracheal tube and the anaesthesia circuit to allow passage of the bronchoscope, oxygenation, ventilation, and maintenance of anaesthesia without contaminating the environment with waste gases. In animals that are too small to allow passage of the bronchoscope through the endotracheal tube, anaesthesia must be maintained with an injectable anaesthetic. Propofol in 1 mg/kg increments for induction plus a constant rate infusion (CRI) of 0.1–0.4 mg/kg/min is recommended; care must be taken not to cause apnoea at induction and during the CRI; careful titration is key. When using the latter technique, oxygen supplementation may be provided through a small soft rubber tube (a urinary catheter works well) passed into the trachea. After the end of the procedure, the animal is usually intubated and the tube is left in place until the gag reflex has returned.

Pleural effusion/pneumothorax: Pleural effusion and pneumothorax dramatically impact the mechanics of ventilation, leading to hypoventilation, atelectasis and hypoxaemia. These patients may be very unstable, and stress caused while obtaining diagnostic radiographs or draining the pleural space may cause decompensation. For this reason, oxygen supplementation is necessary and often some degree of sedation is needed. Butorphanol (0.2–0.4 mg/kg i.v. or i.m.), with or without midazolam (0.2 mg/kg i.v. or i.m.) can be used safely.

Central nervous system

Seizures: Seizures represent a common neurological emergency; however, the optimal treatment strategy is still a topic of debate. Levetiracetam, phenobarbital and benzodiazepines (midazolam if prolonged infusions are necessary) are the initial treatments of choice in small animals, with propofol added if these fail.

Increased intracranial pressure: Increased ICP leading to vascular compression and cerebral anoxia, can arise as a secondary complication of head trauma, cerebral haemorrhage, space-occupying brain lesions and cerebral oedema. Sedation or anaesthesia in these patients carries considerable risk of acute elevation of ICP and rapid deterioration of cerebral function. This may become clinically evident with the manifestation of a Cushing's reflex (hypertension and reflex bradycardia). Care must be taken that hypoventilation does not occur when administering anaesthetic drugs to these patients. Close monitoring of the arterial partial pressure of carbon dioxide (P_aCO_2) is warranted and mechanical ventilation should be instituted to maintain values of 32–35 mmHg (mild hyperventilation). Inhalational anaesthetics above 1 multiple of minimum alveolar concentration (MAC) and ketamine at anaesthetic doses are contraindicated, and opioids (respiratory depression), especially pure mu agonists, must be used carefully. Propofol, thiopental and benzodiazepines are the anaesthetic drugs most commonly used (Figure 21.6).

Treatment	Dose	Comments
Hyperventilation	P_aCO_2 30–35 mmHg	• Do not decrease P_aCO_2 below 28 mmHg as excessive cerebral vasoconstriction may cause brain hypoxia
Mannitol	0.5–1.0 g/kg i.v.	• Has to be given slowly over 10–15 minutes • Contraindicated if cerebral haemorrhage is suspected • Short duration (4–6 hours), replace fluid losses from osmotic diuretic effect
Hypertonic saline 5–7%	4 ml/kg i.v.	• Indicated if cerebral haemorrhage is present • Usually only one dose is given because of risk of hypernatraemia with repeat doses
Elevate head by 30 degrees		• Avoid bending the neck, which would compress the jugular vein, causing increased intracranial pressure • Facilitates venous drainage from the brain

21.6 Treatment for an acute increase in intracranial pressure (Cushing's reflex) (see also Chapter 9).

Drugs commonly used for anaesthesia

Ketamine

Ketamine is a phencyclidine anaesthetic that non-competitively antagonizes the ionotropic glutamate NMDA (*N*-methyl-D-aspartate) receptor. Historically, ketamine has been used as a short-acting general anaesthetic, and at low doses it is currently used as an adjuvant analgesic during GA and in the conscious patient. The anaesthetic state produced by ketamine is described as a functional and electrophysiological state of dissociation between the thalamocortical and limbic systems.

Ketamine has the ability to stimulate the cardiovascular system by causing an increase in central catecholamine levels, mainly by inhibiting their re-uptake. Ketamine administration as a general anaesthetic or as an adjunct to inhalational anaesthesia can maintain stable haemodynamic function via sympathetic stimulation in patients with acute hypovolaemic shock. Heart rate, blood pressure and cardiac output are minimally affected or even increased (Fayyaz *et al.*, 2009). However, studies have demonstrated a direct inhibition of the contractile force of the myocardium. For this reason, in critically ill patients which have the potential for catecholamine depletion, the beneficial indirect cardiovascular effects of ketamine may be absent and the direct myocardial inhibition may manifest itself. In one study, cardiac output decreased more during haemorrhage and hypovolaemia in humans anaesthetized with ketamine than in those anaesthetized with isoflurane. Higher lactate concentrations were also detected in the patients anaesthetized with ketamine since oxygen demands were probably not met with this protocol (Weiskopf *et al.*, 1981). In dogs, ketamine is extensively metabolized to active and inactive compounds by the liver, whilst in cats the drug is primarily eliminated in its active form by the kidneys. Care must be taken when administering ketamine in cats with impaired renal function, as the duration of action may be dramatically increased (Figure 21.7).

Ketamine uses	Dose	Comments
Premedication	2–5 mg/kg i.m. 5–10 mg/kg orally	• Not to be used alone (causes muscle rigidity and tremors) • Use with midazolam, acepromazine or (dex)medetomidine • Aggressive cats: it can be effective if squirted into the mouth
Induction/ maintenance of anaesthesia	2–5 mg/kg i.v. ± 1–3 mg/kg/h 2 mg/kg + 0.5–1 mg/kg propofol i.v.	• Used in combination with midazolam or diazepam • Used in combination with propofol to reduce cardiovascular effects • Used as a CRI ketamine has potential for accumulation
Inhalational anaesthetic MAC sparing	0.5–1 mg/kg bolus i.v. + 0.5–1 mg/kg/h	• To reduce the cardiovascular and respiratory depressant effects of inhalational anaesthetics

21.7 Commonly used doses of ketamine in the dog and cat. CRI = constant rate infusion; MAC = minimum alveolar concentration.

Indications:

- Patients with bradyarrhythmias (second- and third-degree AV block, atrial standstill).
- MAC sparing properties for inhalational anaesthetics.
- Hypovolaemia and sepsis.

Contraindications:

- Cats with impaired renal function.
- Cats with hypertrophic cardiomyopathy.
- Dogs with aortic or pulmonic stenosis.
- Dogs with decreased liver function.
- Dogs and cats with depleted catecholamine stores.
- Dogs and cats with seizures.
- Dogs and cats with increased ICP.
- Dogs and cats with increased intraocular pressure.

Propofol

Propofol (2,6-diisopropylphenol) is a non-barbiturate, short-acting hypnotic agent primarily used for induction and maintenance of GA. Due to its high lipid solubility and water insolubility it is formulated in an aqueous–lipid emulsion (1%) that consists of 10% soybean oil, 2.25%

glycerol and 1.2% egg lecithin. It is stable at room temperature and is not light sensitive; however, as it contains no preservatives (except PropoFlo 28®) and promotes bacterial growth, the shelf-life once the vial has been breached is extremely short at 6–12 hours depending on the formulation. The action of propofol is mediated by its interaction with specific components of the $GABA_A$ (gamma-aminobutyric acid) receptors, causing brain and spinal cord depression with minimal to no analgesia. The onset of action once administered intravenously is rapid, but not as rapid as thiobarbiturates.

Cardiovascular and respiratory depressant effects are dose dependent and closely associated with the speed of injection. These include: decrease in mean arterial blood pressure due to the combination of vasodilation and decreased myocardial contractility; decrease in baroreceptor reflex; enhancement of the arrhythmogenic effects of adrenaline (epinephrine); decrease in tidal volume, respiratory rate and ventilatory response to CO_2. As far as the central nervous system (CNS) is concerned, propofol has neuroprotective properties comprising a decrease in the cerebral metabolic rate, cerebral blood flow and ICP. The duration of effect after a single bolus is around 10–15 minutes and remains similar even after repeated boluses or prolonged infusions (minimal accumulation). This is due to a very short plasma half-life caused by rapid redistribution and extensive metabolism (hepatic and extrahepatic). In the cat the plasma half-life of propofol is longer than in the dog, especially after prolonged infusions, and the duration of effect is usually longer (20 minutes). The use of propofol in the cat may cause the formation of Heinz bodies in red blood cells; however, this is usually of little concern if a single dose is administered and this phenomenon is still considered controversial, with contrasting studies present in the literature (Andress *et al*., 1995; Bley *et al*., 2007).

Care must be taken when administering this drug to patients with cardiovascular instability; careful slow titration is highly recommended, and the use of co-induction agents (opioids, benzodiazepines and lidocaine) with the goal of reducing propofol requirements is a common practice (Sánchez *et al*., 2013) (Figure 21.8).

Propofol uses	Dose	Comments
Induction of anaesthesia	0.5–1 mg/kg i.v. (slow) incremental to effect. Doses up to 6 mg/kg may be required depending on premedication	• Slow incremental boluses will decrease the incidence of cardiovascular depression and apnoea • Fentanyl at 2–5 μg/kg and midazolam or diazepam at 0.2 mg/kg can be used as co-induction agents • With benzodiazepines as a co-induction agent administer 1 mg/kg propofol first to avoid paradoxical excitement
Maintenance of anaesthesia	0.1–0.5 mg/kg/min CRI	• If used alone it provides no analgesia • Palpebral reflexes are usually maintained (if absent, patient is too deeply anaesthetized) • Respiratory depression may require mechanical ventilation
Total intravenous anaesthesia	0.1–0.3 mg/kg/min CRI ± fentanyl at 0.1–0.3 μg/kg/min ± ketamine at 0.5–2 mg/kg/h	• Fentanyl and ketamine reduce the minimum infusion requirements of propofol, reducing cardiovascular effects and providing analgesia

21.8 Commonly used doses of propofol in the dog and cat. CRI = constant rate infusion.

Indications:

- Decreased liver or renal function.
- Sighthounds.
- Induction agent for Caesarean section (Moon *et al*., 1998).
- Intracranial disease with increased ICP (with mechanical ventilation).
- Total intravenous anaesthesia (TIVA).
- Treatment of seizures refractory to first-line treatment.

Contraindications:

- Cardiovascular instability.
- Hypovolaemic patients.
- Repeated doses or prolonged infusions in anaemic cats.

Alfaxalone

Alfaxalone is a synthetic neuroactive steroid used for induction and maintenance of GA in dogs and cats. The previous formulation of this drug was a mixture of alfadolone and alfaxalone, which, due to its water insolubility, was formulated in Cremophor®. The latter caused severe histamine release and anaphylactic reactions, prompting its withdrawal from the market. The modern formulation of alfaxalone owes its water solubility to a molecule of cyclodextrin which does not cause histamine release and is metabolized by the liver.

Pharmacological characteristics include rapid onset of action (faster than propofol), minimal cardiovascular and respiratory depressant effects when given at therapeutic doses, wide margin of safety (Muir *et al*., 2008), short duration of action, no analgesic properties, and little accumulation if repetitive doses or long infusions are administered. Because of its cardiovascular sparing properties alfaxalone may be suitable for critically ill patients. Unlike propofol it can be administered, intramuscularly to cats and small dogs; therefore it can be used for sedation in unstable patients that require tranquillization for intravenous access and restraint. It is not suitable for intramuscular injection in larger dogs due to the volume of fluid that would need to be administered. In cats that have received alfaxalone without any premedication, recoveries may be characterized by emergence delirium, especially if they take place in a loud and bright environment. Alfaxalone may be a suitable alternative to etomidate in critically ill patients when the potential for adrenal suppression due to etomidate administration is a major concern. As with propofol this drug does not contain any antimicrobial preservatives, therefore the labelling mandates discarding any remaining drug following withdrawal of the required dose, or at the end of the day (label varies among different countries). However, unlike propofol, alfaxalone does not promote bacterial and toxin development (Figure 21.9).

Indications:

- Cardiovascular instability.
- Intramuscular sedation of unstable stressed cats for intravenous catheterization.
- Induction agent for Caesarean section.
- Sighthounds.
- Repetitive dosing and infusions in cats (Warne *et al*., 2015).

Contraindications:

- Emergence delirium from anaesthesia.
- If given rapidly, a period of apnoea is commonly seen (dose dependent).

Alfaxalone uses	Dose	Comments
Induction of anaesthesia	Dogs: 1–3 mg/kg i.v. (slow) to effect Cats: 2–5 mg/kg i.v. (slow) to effect	• Slow boluses will decrease the incidence of apnoea • Use a benzodiazepine as co-induction agent for smoother loss of consciousness and intubation
Maintenance of anaesthesia	Dogs: 4–7 mg/kg/h CRI Cats: 5–8 mg/kg/h CRI	• No analgesia if used alone, commonly combined with fentanyl CRI
Sedation in cats	1–3 mg/kg i.m. + midazolam at 0.2 mg/kg i.m. and/or butorphanol at 0.2 mg/kg i.m.	• Never use alone, high volume limits its use • Alternative to ketamine i.m. in unstable patients; useful in cats as premedication when acepromazine or (dex) medetomidine are not indicated, short duration but enough to place i.v. catheter

21.9 Commonly used doses of alfaxalone in the dog and cat. CRI = constant rate infusion.

Etomidate

Etomidate is a carboxylated imidazole derivative with hypnotic effects and a short duration of action, commonly used for the induction of anaesthesia. Due to its minimal cardiovascular and respiratory depressant effects, etomidate is routinely used in dogs and cats that show considerable cardiovascular instability/disease. Pharmacokinetic characteristics include rapid uptake, clearance, and metabolism to a pharmacologically inactive metabolite by hepatic microsomal enzymes. Like propofol and barbiturates, it interferes with the $GABA_A$ receptor, enhancing the inhibitory effects of the endogenous neurotransmitter GABA. Etomidate decreases intraocular pressure and ICP making it a suitable induction agent for ocular and neurological emergencies in patients with cardiomyopathies. Although etomidate may raise the threshold for generalized seizure activity, it lowers the threshold for focal seizure activity; this raises some concerns for the use of this drug as an anticonvulsive.

The most distinctive property of etomidate compared with propofol and thiobarbiturates is its minimal effect on heart rate, mean arterial blood pressure, stroke volume and systemic vascular resistance (Pascoe *et al*., 1992). Even compared with other induction drugs its respiratory effects are minimal, although short episodes of apnoea (20 seconds) may be observed during the induction of critically ill patients. The most significant concern regarding the use of etomidate in the emergency patient is its inhibitory effect on adrenal function and specifically on corticosteroid production. In human ICU patients that received a single dose or long-term infusions of the drug there was a dramatic increase in morbidity and mortality linked to adrenal insufficiency (Annane, 2005). In dogs that receive etomidate as an induction agent adrenal function is suppressed for 2–6 hours after induction; for this reason care must be taken when using this drug in severely debilitated animals where adrenocortical function is already suppressed, and supplementation with a short-acting glucocorticoid may be indicated in these patients (Figure 21.10). Retching is also another significant concern with the administration of etomidate.

Etomidate uses	Dose	Comments
Induction of anaesthesia	0.3–0.5 mg/kg i.v. slow bolus to effect	• If using the hyperosmolar formulation (USA) it has to be diluted for use in cats • In patients with head trauma it is preferred to propofol or thiobarbiturates because it does not decrease MAP and maintains cerebral perfusion pressure

21.10 Commonly used doses of etomidate in the dog and cat. MAP = mean arterial pressure.

Indications:

- Cardiovascular instability.
- Ketamine.
- Patients with increased intraocular pressure.
- Patients with increased ICP.

Contraindications:

- Adrenocortical suppression.
- Septic patients.
- Focal seizures.

Inhalational anaesthetics

The most commonly used inhalational anaesthetics in veterinary medicine are isoflurane, sevoflurane, desflurane and halothane. Potency of this class of drug is conventionally expressed in terms of MAC. MAC is defined as the end-tidal concentration, expressed as a percentage, of an inhalational anaesthetic that prevents movement in response to a supramaximal noxious stimulus in 50% of the studied individuals. MAC is considered a valuable measurement, especially in recent years, for quantifying the effects of injectable anaesthetic drugs on reducing requirements for inhalational anaesthetics (Figure 21.11). Since cardiovascular depression by these drugs is dose dependent, the synergistic use of parenteral drugs (fentanyl, ketamine, lidocaine, (dex)medetomidine) decreases the amount of inhalational anaesthetic needed, therefore benefiting haemodynamic function.

Many factors reduce MAC (inhalant) requirements and should be taken into account when using inhalational anaesthetics. These include age, hypothermia, depressed cardiovascular function, depressed mentation, hypercarbia, metabolic acidosis and pregnancy.

Inhalational anaesthetic	MAC dog	MAC cat	Comments
Halothane	0.8%	1.0%	• Most cardiovascular depressant, least respiratory depressant, arrhythmogenic
Isoflurane	1.2%	1.6%	• Airway irritation, 0.2% metabolized, may increase heart rate
Sevoflurane	2.2%	2.6%	• No airway irritation, 4% metabolized, toxic compound A produced in soda-lime at low flows
Desflurane	7.5%	10.2%	• Fastest recovery, least metabolized at 0.02%, requires a special heated (39°C) vaporizer, not indicated for mask inductions

21.11 Minimum alveolar concentration (MAC) of inhalational anaesthetics and specific characteristics in the dog and cat.

All inhalational anaesthetics cause severe dose-dependent cardiovascular and respiratory depression, and have no analgesic properties. Halothane is the most cardiovascular depressant of all the inhalational anaesthetics, and also causes myocardial sensitization to catecholamines, causing arrhythmogenicity. For these reasons, and because better alternatives are available, halothane is contraindicated in ill and debilitated patients. In general, care must be taken when using inhalational anaesthetics in ill and debilitated patients as they may not tolerate the negative cardiovascular effects such as hypotension.

The precise mechanism by which inhalational anaesthetics depress the CNS is still unknown; however, there is strong evidence that this is mediated by the alteration of synaptic cellular membrane permeability and interference with numerous receptors present in the CNS (Na^+, Ca^+ channels and GABA receptors). The greatest advantage of inhalational anaesthetics is that these drugs are administered and eliminated through the respiratory system and for the most part they do not accumulate in tissues or require hepatic metabolism, with the exception of halothane. For this reason, even after prolonged anaesthetic events, recovery is rapid and predictable.

Indications:

- Patients with stable cardiovascular function.
- Hepatic insufficiency.
- Renal insufficiency.

Contraindications:

- Patients with unstable cardiovascular function.
- Head trauma (unless used at concentrations below 1 MAC).
- Increased ICP.

Induction of anaesthesia

The induction of anaesthesia, along with the recovery period, is probably the event that presents the most risk and potential complications in the critical patient (Brodbelt *et al*., 2008). During this phase the administration of anaesthetic drugs dramatically changes the physiological homeostasis of the cardiovascular, respiratory and nervous systems. A checklist approach is useful in preparation for this critical event, taking into consideration the specific conditions, needs and concerns for the patient (see 'Useful links'). Being prepared for a complication is part of the solution.

- Check that the anaesthesia machine, oxygen supply and monitoring equipment are functioning correctly.
- Check that one or two routes for venous access are patent and well secured in place.
- Verify the presence of all drugs needed for induction, considering extra doses and flushes.
- Verify the presence of all the materials necessary for endotracheal intubation: different tube sizes, laryngoscope, stylets (if difficult airway), syringe for cuff inflation, and means to secure the tube in place.
- Calculate and check availability of emergency cardiovascular drugs and relevant reversal agents.
- Place relevant monitoring instruments on the patient (electrocardiogram (ECG) leads, Doppler probe, blood pressure cuff and pulse oximeter, when possible).
- Pre-oxygenate with facemask delivering 100% oxygen for 3 minutes.

The importance of these preliminary operations should not be underestimated regardless of the specific condition of the critical patient. If for some reason instrument placement and pre-oxygenation is not tolerated, administer fentanyl (2–5 μg/kg i.v.) or propofol (0.2–0.5 mg/kg i.v.) as a sedative. A Doppler probe present during induction is highly recommended. It allows measurement of baseline arterial blood pressure, and rapid detection of changes in arterial blood flow and pulse rhythm in case of cardiovascular collapse at induction.

The type of induction drug regimen will be dictated by the specific condition of the patient. In general, careful titration of anaesthetic drugs is warranted, keeping in mind that it is simpler to administer additional doses of a specific drug than deal with the complications that arise from overdosage. In patients with severe cardiovascular compromise, induction of anaesthesia with fentanyl (3–5 μg/kg i.v.) and diazepam (0.2 mg/kg i.v.) is a safe option.

Maintenance of anaesthesia

During anaesthesia of the critical patient, it is of crucial importance to continuously monitor vital parameters such as heart rate, rhythm, respiratory rate, tidal volume, temperature, haemoglobin oxygen saturation, end-tidal carbon dioxide ($ETCO_2$) and arterial blood pressure. The anaesthetist must constantly intervene when parameters deviate from physiological or desired values. All values should be recorded on a standardized anaesthetic record sheet (Figure 21.12).

Hypothermia, hypotension and metabolic acidosis are common complications that arise during GA and should be treated promptly. All attempts should be made to maintain temperature within normal ranges. Circulating warm water blankets should be used to isolate the patient and prevent loss of heat through the table surface, and patients should be covered with forced air warming devices (Bair Hugger®). If it is not possible to cover the patient because of surgical field contamination, use specific blankets that go under the patient or infrared warming devices that work without direct contact with the animal (Figure 21.13). Exposed viscera should be covered with warm damp gauzes to avoid heat loss through evaporation, and warm fluids should be used to lavage open body cavities.

The risk of hypotension due to cardiovascular depressant drugs should be addressed by combining different drugs that act synergistically to reduce the overall side effects (fentanyl CRI, ketamine CRI, midazolam CRI or lidocaine CRI to decrease the MAC of inhalants). It is important to keep track of circulating fluid volume losses and correct them appropriately. Finally, if necessary, vasopressors should be used to support the cardiovascular system (Figure 21.14).

Cardiovascular monitoring

Cardiovascular monitoring is of crucial importance in the critical patient. There is no doubt that the continuous monitoring of cardiovascular parameters such as heart rhythm, heart rate and arterial blood pressure has made anaesthesia safer. However, the ability to monitor these patients with our own senses should never be lost or ignored. The anaesthetist should always be suspicious of values that do not correlate with clinical signs. Also there is a need to bear in mind that many automated devices that measure non-invasive blood pressure are tested using healthy individuals with normal heart rates and rhythms. For this reason these monitors may have a certain degree of error

Anaesthesia codes

- ▼ Doppler
- ● Pulse rate
- ▼ Systolic B.P.
- ▲ Diastolic B.P.
- – Mean B.P.
- ○ Respiratory rate
  Spont (S) Manually assist (A) Mechanical (M)
- × Start – end anaesthesia
- ◉ Start – end surgery

Date:

Location/or:

Dr. Ao: Tech:

Patient information:

Heart murmur Grade____/VI Type_____

Arrest code: Green Yellow Red (circle)

PCV_____ TP_____Dex. _____Azo. _____

T._____ P._____ R._____ WT_____kg

History and current therapy:

Procedure _____

Clinician _____Anaesthetist_____

Position/s _____Blood loss_____ml

Number sponges before surgery: _____ After surgery:_____

Total fluids

_____ml
_____ml
_____ml
_____ml
_____ml

Anaesthesia time

_____hrs_____ mins

Procedure time

_____hrs_____ mins

ECG: ☐Yes ☐No	Drug	Code	AMT mls	Dispenser
i.v. cath: Loc:				
i.v. cath: Loc:				
Art cath: Loc:				
Oth cath: Loc:				
BP: Direct: Indirect:				
Cuff: ☐Doppler ☐NIBP				
Pre-anaesthetic state:				
P.S. 1 2 3 4 5 E (circle)				
☐Anxious ☐Calm ☐Excitable				
☐Depressed ☐Other				

Epidural _____ Spinal_____

Block _____ Attempts_____

Location:_____

CSF ☐Yes ☐No Blood ☐Yes ☐No

Catheter ☐Yes ☐No

Needle: G ___ L ____Stim. needle_____

Administrator:_____

Drug	mg	ml

Pre-anaesthetic: Route: Time: Endo size:

Effect: HR: RR: Endo attempts:

Induction drugs in mgs:

ISO. SEVO. DES ET %																								
O_2/min																								
$ETCO_2$																								
S_pO_2																								
Fluids:																								
Temp°C ☐AX ☐R ☐O																								
Time: ☐am ☐pm																								
200																								200
190																								190
180																								180
170																								170
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50																								50
40																								40
30																								30
20																								20
10																								10
0																								0
Vent S A M (circle one)																								
Tidal vol (ml)																								
PIP/PEEP																								

Position ☐ Sternal ☐ Dorsal ☐ Left lat ☐ Right lat

Notes

Recovery score
☐ 1 Good
☐ 2
☐ 3
☐ 4
☐ 5 Poor
T_____
P_____
R_____

21.12 Example of an anaesthesia record.



21.13 Infrared heat lamp, used when heating devices that require direct contact with the patient cannot be used because of the surgical field.

when used in animals with severely deranged cardiovascular parameters.

In the operating room the best way to assess heart rate and rhythm is with the use of an ECG. Most of the time only three leads are necessary and they can be placed in different positions as long as they form a triangle around the heart. This will allow immediate detection of the most common arrhythmias during the anaesthetic, and guide treatment.

The body has the ability to autoregulate tissue perfusion across a range of mean arterial blood pressures (60–150 mmHg). However above and below these values tissue perfusion varies linearly with mean arterial pressure. Arterial blood pressure monitoring enables the estimation of tissue perfusion, and when integrated with other cardiovascular parameters it relates important information on cardiovascular performance. Also, during surgical manipulation it becomes a useful tool for monitoring the sympathetic response of the patient, giving valuable information on the effectiveness of analgesic regimens and the depth of anaesthesia.

Arterial blood pressure itself will give little information on the volume status of the critical patient. However, during mechanical ventilation, pulse pressure variation detected by rhythmic fading of the Doppler intensity or via multiparameter monitors is a clear sign of volume depletion and fluid responsiveness. In the critical patient arterial blood pressure is preferably measured invasively, by placing an arterial catheter most commonly in the dorsal pedal artery of dogs and cats (see Chapter 2). This technique carries numerous advantages, such as continuous 'beat-by-beat' assessment, the ability to assess the impact of arrhythmias on tissue perfusion, provision of accurate arterial blood pressure measurements even in the presence of hypotension, and convenience as a blood-sampling site. Disadvantages include complexity of arterial catheterization, haematoma formation, expensive equipment and infection.

When direct measurement of arterial blood pressure is not feasible, the authors recommend the Doppler technique (Figure 21.15) for blood pressure monitoring, which has been proven to be more accurate and useful in the hypotensive patient than the oscillometric technique (Dyson, 2007; Kennedy and Barletta, 2015).

Cardiac output is the volume of blood ejected by the right ventricle each minute. Its measurement precisely evaluates cardiac performance and is fundamental in deriving indices that better quantify perfusion such as oxygen delivery, oxygen consumption and oxygen extraction ratio. Historically, cardiac output has not been measured in clinical practice due to the invasiveness of the technique and the cost. Recently, new non-invasive and cost-effective options have become available for clinical use. The NiCO® is a non-invasive cardiac output monitor that utilizes CO_2 rebreathing and may be used in clinical practice (Figure 21.16). Limitations of its use include patient size (>15 kg), and the need for mechanical ventilation and arterial blood gases for calibration.



21.15 Septic dog under general anaesthesia being monitored via ECG, Doppler (blood pressure), S_pO_2 and end-tidal gases.

Sympathomimetic	Dose	Adrenoreceptor	Effect
Dopamine	Low: 1–4 μg/kg/min CRI Medium: 5–10 μg/kg/min High: >10 μg/kg/min	Low to medium dose dopamine, beta-1 effects; alpha-1, alpha-2 effects at high dose	Low dose: renal vasodilation Medium dose: increased CO High dose: vasoconstriction
Dobutamine	1–5 μg/kg/min CRI	Beta-1(+++) and beta-2(++)	Increases CO, if higher doses are used it will increase HR; vasodilatory effect so no increase in BP
Noradrenaline (norepinephrine)	0.1–1.0 μg/kg/min CRI	Potent beta-1, alpha-1, alpha-2	Increase in BP and minimal change in HR or CO Combine with dobutamine to increase CO Used in refractory hypotension
Ephedrine	0.1–0.2 mg/kg bolus	Indirect acting synthetic non-catecholamine, causes endogenous release of noradrenaline	Increase in BP and CO, short acting – 15 minutes, second dose ineffective, causes CNS stimulation
Phenylephrine	0.1–0.5 μg/kg/min	Potent alpha-1	Potent vasoconstrictor, increases BP solely by increasing systemic vascular resistance

21.14 Characteristics and doses of commonly used sympathomimetics during general anaesthesia. BP = blood pressure; CNS = central nervous system; CO = cardiac output; CRI = constant rate infusion; HR = heart rate; ++ = minor degree of affinity to the receptor; +++ = moderate degree of affinity to the receptor.



21.16 NiCO® cardiac output monitor (Respironics, Carlsbad, CA, USA).

Oxygenation and ventilation

Respiratory depression, or more often the complete abolition of ventilation, is commonly induced by GA. Additionally, the machine and anaesthetic circuit have the potential to fail. Thus, many anaesthesia-related complications arise from problems associated with respiratory function. This is especially true in the critically ill patient, where the lack of physiological reserves and compensatory mechanisms tends to increase the occurrence of critical complications.

The use of pulse oximetry and capnometry/capnography allows non-invasive, continuous and real-time monitoring of oxygenation and ventilation. Pulse oximetry measures the haemoglobin oxygen saturation in arterial blood and indirectly reflects the partial pressure of oxygen (P_aO_2). Unfortunately, pulse oximetry alone fails to give any information on the oxygen content of the blood, and this can become problematic in severely anaemic or hypovolaemic patients, where normal values of pulse oximetry may give the false security of appropriate oxygen delivery to the tissues. For this reason it is advisable in the anaemic patient to relate pulse oximetry to haemoglobin content and blood gas analysis in order to clearly understand and devise a treatment strategy.

Capnometry consists of the measurement of the partial pressure of CO_2 in expired gases, while capnography represents the partial pressure of CO_2 over time in the form of a wave. Many aspects of ventilatory function can be derived from this monitoring technique. The height of the wave reflects the P_aCO_2, providing information on hypoventilation or hyperventilation (see Chapter 7). The frequency of the wave reflects respiratory rate and in most monitors it is displayed digitally. The baseline gives critical information on rebreathing, which can be caused by failure of the soda-lime canister, low flows, or mechanical failure of the anaesthesia machine or circuit. The morphology and trends give information on patient disconnection, leaks in the system, dramatic increases and decreases in cardiac performance and obstruction of the tracheal tube. Normal and abnormal capnograms can be found at the website www.capnography.com.

Modern monitors and ventilators measure spirometry, which allows accurate evaluation of tidal volumes, compliance and resistance of the pulmonary system. In patients with pulmonary disease and severe cardiac compromise, capnometry may not accurately reflect P_aCO_2. For this reason, when anaesthetizing these patients blood gas analysis is warranted in order to verify appropriate ventilatory function and validate the values obtained with the capnometer.

Acid–base balance and electrolytes

Blood gas analysers provide information on oxygenation and ventilation, and also accurate information on electrolyte and acid–base status. Blood may be sampled through previously placed arterial lines or by direct stick of an artery (dorsal pedal, lingual and femoral).

Acid–base balance and electrolytes should be monitored during anaesthesia of the critical patient, especially during long procedures and for patients that receive considerable volumes of fluids or blood products. Special emphasis should be directed at K^+, ionized Ca^{2+}, Mg^{2+}, glucose, lactate, pH, P_aCO_2 and base excess (see Chapter 5). Frequent blood gas analysis will allow rapid detection of relevant derangements and monitoring of efficacy of treatment.

Recovery from anaesthesia

Recovery from anaesthesia carries many potential complications that warrant close monitoring and intervention. In this phase the patient is usually hypothermic, transitioning from 100% oxygen to room air, still affected by residual traces of anaesthetic gases, and has relevant plasma levels of anaesthetic drugs (opioids, benzodiazepines, ketamine).

Active and passive warming should be continued until the patient can spontaneously maintain normal body temperature. Respiratory and cardiovascular function should be monitored. Arrhythmias that develop during the recovery phase may not be identified if the ECG cables have been disconnected, or if the patient is moving around and no longer tolerates them. If the patient has received considerable doses of opioids and/or benzodiazepines, ventilation or the gag reflex (the ability of the patient to control its airway) may be depressed, and reversal should be considered (Figure 21.17). It is important to evaluate closely the pain status of the patient, differentiating pain from dysphoria, and then devise an appropriate management strategy.

Anaesthetic drug	Reversal agent and dose	Comment
Benzodiazepines	Flumazenil at 0.01–0.1 mg/kg i.v.	Scientific studies on doses for dogs and cats are lacking: start with low dose, short duration (45 minutes), redose if necessary
Opioids	Naloxone at 0.01–0.04 mg/kg i.v. Butorphanol at 0.02–0.05 mg/kg i.v.	Titration is essential in order to preserve analgesia Butorphanol more effective in preserving analgesia Short duration (45 minutes), potential for re-narcotization

21.17 Reversal agents for opioids and benzodiazepines and their uses.

Analgesia in the critical patient

According to the International Association for the Study of Pain (IASP), pain is 'an unpleasant sensory and emotional experience, associated with actual or potential tissue damage, or described in terms of such damage'. Pain produces a series of undesirable effects:

- It may increase the post-injury stress response and sympathetic nervous system activity
- It causes behavioural changes, immunosuppression and altered food intake, and increases catabolism
- It can increase morbidity and mortality while delaying healing and hospital discharge
- It compromises animal welfare.

Pain assessment must be considered as part of the physical examination as the fourth vital sign, especially in emergency and critical care. Treatment of pain may prevent complications including the development of hyperalgesia, central sensitization and allodynia.

General considerations

Analgesia in emergency and critically ill patients may be required for a variety of painful conditions that can include:

- Non-surgical (medical) and surgical emergencies (i.e. pancreatitis, gastric dilatation–volvulus, urinary obstruction, diaphragmatic hernia and Caesarean section)
- Trauma emergencies (i.e. road traffic accident, bladder rupture, haemoabdomen/haemothorax, fractures)
- Perioperative care (i.e. spinal surgery, thoracotomy, limb amputation).

In critically ill patients, dogs and cats present different disease processes that can affect drug absorption, distribution, metabolism and elimination. Analgesic efficacy may be less than optimal, or because of decreased organ function there may be a greater than normal response to a standard dose, and narcosis can occur. Analgesics should be administered on a case-by-case basis, and are often required immediately after the first physical examination.

In addition to the primary cause of pain, the presence of other concomitant diseases/drug therapies must be considered, and therapy tailored to the individual. For example, obesity can increase the percentage of fat tissue over the lean mass, increasing the volume of distribution for lipophilic drugs into tissues that are not metabolically active. Therefore, doses should be reduced and/or calculated according to an estimation of lean bodyweight in obese dogs and cats (Figure 21.18). This approach will avoid overdosing and potential adverse effects. On the other hand, neonates, paediatric and geriatric patients have physiological differences that affect pharmacokinetics in comparison with the adult individual. Analgesic dosage regimens should be adjusted according to age, breed, body condition, temperament, target effect, disease process and efficacy of analgesia.

Adequate treatment of pain usually requires proper recognition of pain behaviours (Figure 21.19). It may be challenging to recognize pain in the critically ill patient, as these animals are often depressed, lethargic and/or stuporous. Furthermore, most pain scoring systems have been developed and validated in healthy dogs or cats undergoing surgery and/or anaesthesia, and may not be appropriate in critically ill patients. However, a validated pain scoring system in cats has recently been published and it provides a useful tool for the diagnosis and treatment of pain after ovariohysterectomy (Brondani *et al*., 2013). In addition, the Glasgow feline pain scoring system has been partially validated and can be used in cats with medical or surgical pain (Reid *et al*., 2017). Physiological changes (heart and respiratory rate, cortisol levels, pupil size) contribute little to pain assessment in cats. In dogs, the short-form of the Glasgow pain scoring system can be easily implemented in the emergency setting for practical and rapid canine pain assessment (Reid *et al*., 2017). An interactive approach with gentle palpation of the affected area is recommended during examination. Routine pain assessment is crucial for successful analgesic therapy.

In addition to the classic analgesic plan using traditional analgesics, excellent nursing care is essential to reduce stress and discomfort induced by hospitalization (Figure 21.20). Emptying of the urinary bladder, proper positioning and padding, maintenance of normothermia (unless contraindicated) and anxiolysis are all part of case management. Antiemetics should be given if nausea and vomiting are present. Environmental enrichment is used to reduce stress and anxiety. Pheromone therapy has proven to be helpful in hospitalized cats (Kronen *et al*., 2006). Good surgery technique is important to prevent excessive tissue damage and inflammation.



21.18 Obese cat: analgesia should be based on the estimated lean body mass.



21.19 Typical posture and facial expression in a painful cat.



21.20 Dog in ICU receiving appropriate care in order to minimize stress and discomfort (padding, urinary catheter, dry and warm bedding).

A panel of experts has now provided guidelines on the recognition, assessment and treatment of pain in canine and feline patients (Mathews *et al*., 2014). This open-access document offers additional information on pain management in small animals.

Drugs and analgesic techniques

Drugs such as opioids, lidocaine, ketamine and/or (dex)-medetomidine have been used extensively as either loading doses/boluses or as an infusion. Loco-regional anaesthesia provides excellent pain control in the perioperative period. Non-steroidal anti-inflammatory drugs (NSAIDs) may play a significant role in the prevention and treatment of pain, especially in inflammatory conditions. Drugs such as tramadol and gabapentin may be required when the patient returns to its home and to treat maladaptive (i.e. chronic) pain.

Multimodal analgesia is characterized by the simultaneous use of two or more different classes of analgesics where each class of analgesic acts at different levels of the nociceptive input pathway and has a different onset and duration of action (Kehlet and Dahl, 1993). The synergy among these various pharmacological agents allows clinicians to use lower doses of each drug, and therefore the risk of adverse effects is lower. This can improve analgesia by targeting different receptors and neurotransmitters that participate in the pain pathway.

Attenuation of postoperative pain is best achieved with preventive administration of analgesics. The preoperative use of opioids and local anaesthetics and/or NSAIDs is recommended to prevent central sensitization, and to reduce intraoperative analgesic requirements and anaesthetic-induced cardiopulmonary depression in critically ill dogs and cats undergoing surgery.

Opioids

Opioids are drugs with opiate-like activities, which vary in their receptor specificity, potency and efficacy, resulting in different clinical effects. They bind to opioid receptors (mu (μ), kappa (κ) and delta (δ) and nociceptin/orphanin FQ peptide receptor and their subtypes) in the central and peripheral nervous system. They inhibit the release of excitatory neurotransmitters from afferent fibres in the spinal cord, while causing neuronal hyperpolarization. Due to their potential as drugs of abuse in humans, their use in most jurisdictions is tightly controlled and veterinary surgeons (veterinarians) should adhere closely to the relevant legislative requirements for recording their use.

Opioid analgesics are the cornerstone of effective pain management, with the added benefit of reversibility (Figure 21.21). For example, if profound sedation, dysphoria and/or respiratory depression are observed, opioids can be reversed by an opioid antagonist (naloxone or nalmefene), or an agonist-antagonist (butorphanol).

Opioids cause dose-dependent centrally mediated respiratory depression that could be clinically relevant in critically ill patients (Figure 21.21). This adverse effect can be exacerbated by concurrent use of other respiratory depressants such as some injectable and inhalant anaesthetics. However, this should not be a reason to deprive this patient population of appropriate analgesic therapy. Therefore, dogs and cats should be closely monitored during opioid therapy. 100% oxygen should be provided to prevent or treat hypoventilation and hypoxaemia. Positive pressure ventilation or intermittent positive end-expiratory pressure is recommended during surgery when administering high doses of ultra-short-acting opioids (i.e. fentanyl). Opioids also produce an antitussive effect through central inhibition of the cough centre, which may be of relevance in dogs with laryngeal paralysis or pneumonia.

Opioids may induce an increase in vagal tone leading to bradycardia. This effect is not usually of concern in animals that are stable and/or conscious. Anticholinergic administration reverses or prevents opioid-induced bradycardia. Opioids cause minimal depression of the cardiovascular system and are considered to be relatively safe.

Opioids may decrease oesophageal sphincter pressure and increase the incidence of gastro-oesophageal reflux during anaesthesia and the early postoperative period. This may be of clinical relevance in patients with laryngeal paralysis where post-anaesthesia oesophagitis, regurgitation and aspiration pneumonia is of great concern. In these cases, a CRI of metoclopramide is commonly administered in an attempt to increase lower oesophageal sphincter tone.

Buprenorphine (partial agonist of mu (μ) receptors) tends to cause less respiratory depression and dysphoria than hydromorphone or morphine (full agonists). It is less effective as an analgesic than a full agonist, but may provide adequate pain management when used as part of a multimodal analgesic approach with the addition of a NSAID (unless contraindicated) for mild to moderate pain (Figure 21.21). A review including guidelines on the use of buprenorphine in cats has been published (Steagall *et al*., 2014).

Short-acting drugs such as fentanyl or remifentanil, two synthetic mu (μ) agonists, are administered as infusions. Fentanyl produces minimal haemodynamic changes, although bradycardia and mild respiratory depression have been reported. These drugs reduce inhalant anaesthetic requirements by up to 65% in dogs (Steagall *et al*., 2006) and 20% in cats (Steagall *et al*., 2015) and can be given to effect until pain is controlled.

Remifentanil is degraded by non-specific plasma and tissue esterases, which is an advantage in patients with liver and renal disease. Remifentanil has high clearance, which results in short terminal half-life and duration of

Opioid analgesic	Dog dose	Cat dose	Route of administration	Comments
Morphine	0.3–1.0 mg/kg q2–4h	0.2–0.4 mg/kg q4–6h	i.m.	Intravenous administration may result in histamine release and hypotension
Pethidine (meperidine)	3–5 mg/kg q1–2h	3–5 mg/kg q1–2h	i.m.	Same as above
Methadone	0.5–1.0 mg/kg q3–4h	0.2–0.3 mg/kg q4h	i.m., i.v., OTM	Has NMDA receptor antagonist properties. It can be given buccally in cats
Oxymorphone	0.05–0.20 mg/kg q4h	0.03–0.10 mg/kg q4–6h	i.m., i.v.	
Hydromorphone	0.05–0.20 mg/kg q2–4h	0.025–0.10 mg/kg q4–6h	i.m., i.v.	May cause hyperthermia in cats
Tramadol	4–6 mg/kg q6–8h	2–4 mg/kg q6–8h	i.m., i.v., orally	Weak affinity for opioid receptors Noradrenaline (norepinephrine) and serotonin reuptake inhibitor
Fentanyl	Bolus of 2–5 μg/kg + CRI at 3–6 μg/kg/h	Bolus of 1–3 μg/kg + CRI at 2–3 μg/kg/h	i.v.	Doses may be increased for inhalant anaesthetic-sparing effect or for maximum analgesia. A new transdermal formulation is available. See text
Remifentanil	6–12 μg/kg/h	4–6 μg/kg/h	i.v.	Doses may be increased for inhalant anaesthetic-sparing effect or for maximum analgesia. It does not require a bolus
Butorphanol	0.2–0.4 mg/kg q1–2h	0.2–0.4 mg/kg q1–2h	i.m., i.v.	Limited analgesic efficacy in most cases of moderate or severe pain
Nalbuphine	0.3–0.5 mg/kg q2–4h	0.2–0.4 mg/kg q2–4h	i.m., i.v.	Limited analgesic efficacy in moderate or severe pain
Buprenorphine	0.01–0.02 mg/kg q4–8h	0.02–0.04 mg/kg q4–8h	i.m., i.v., OTM (cats)	Can be given buccally to cats
Naloxone (antagonist)	0.04 mg/kg q0.5–1h	0.04 mg/kg q0.5–1h	i.m., i.v.	Titrate to effect when reversing opioid side effects in painful patients
Nalmefene (antagonist)	0.25–0.30 μg/kg q1–2h	0.25–0.30 μg/kg q1–2h	i.m., i.v.	Titrate to effect when reversing opioid side effects in painful patients
For clinical application of opioid reversal: Naloxone (0.04 mg/kg in 10 ml of saline i.v.) can be diluted and given slowly until the desired endpoint is achieved (i.e. treatment of dysphoria or sedation). Analgesic effects are also reversed.				

21.21 Suggested doses of opioid analgesic drugs and their reversal agents in cats and dogs. CRI = constant rate infusion; NMDA = *N*-methyl-D-aspartate; OTM = oral transmucosal.

action. There are no cumulative effects after prolonged infusion, which may decrease the prevalence of dysphoria and allow for early neurological evaluation. Remifentanil reaches plasma concentrations a few minutes after the beginning of infusion, and does not always require a loading dose. The drug is commercially available in a lyophilized form to be diluted in normal saline or 5% glucose solution, which expires 24 hours after reconstitution. The drug has half the potency of fentanyl, and therefore doses are higher (see Figure 21.21). Loading doses of remifentanil are not administered intravenously because they can cause severe episodes of bradycardia up to atrial standstill and they are not necessary since the drug reaches peak plasma concentration after a few minutes of infusion.

The route of administration affects opioid analgesia. Recent studies have demonstrated that analgesia can be insufficient when opioids are administered by the subcutaneous route in cats. In fact, cats failed to achieve adequate plasma concentrations and/or had minimal antinociception after subcutaneous hydromorphone, methadone, morphine and/or buprenorphine. On the other hand, morphine and pethidine (meperidine) should not be administered rapidly by the intravenous route due to potential histamine release followed by hypotension and vasodilation. Pruritus and hypersensitivity reactions can also occur. The buccal or oral transmucosal route has been used for the administration of methadone, buprenorphine and (dex)medetomidine in cats (Figure 21.22). Epidural and transdermal analgesia using opioids are discussed later in this chapter. An extensive review on opioids in small animals has been published (Simon and Steagall, 2017).



21.22 Oral administration of buprenorphine in a cat.

Individual variability after opioid administration has been reported in different species. Variables such as sex, age, genotype and distribution of opioid receptors play an important role in individual pharmacokinetic differences. These variables may determine the response to perioperative analgesic administration and therefore pain should be routinely assessed and therapy tailored to individual needs.

To summarize the clinical use of opioids in the perioperative period:

- Preoperative: administer methadone, morphine or hydromorphone alone, or in combination with midazolam, acepromazine or dexmedetomidine (i.m. or i.v.) as part of premedication
- Intraoperative: high doses of fentanyl or remifentanil to provide and maximize inhalant anaesthetic-sparing effects and pain relief, and produce less cardiovascular depression produced by inhalant anesthetics
- Postoperative: intermittent boluses of hydromorphone or methadone or low doses of fentanyl or remifentanil given to effect. Opioid therapy is best used with other analgesic agents (multimodal analgesia) (see Figure 21.21).

Non-steroidal anti-inflammatory drugs

NSAIDs are the most widely used analgesics in veterinary medicine (Lascelles *et al*., 2005). These drugs have become popular for their anti-inflammatory, analgesic and antipyretic effects, with both central and peripheral activity (Figure 21.23). The analgesic effects of NSAIDs are secondary to the inhibition of cellular expression of cyclooxygenase (COX) enzymes. There are at least two COX isoforms. The COX-1 isoform is believed to be a constitutive form of the enzyme found in many tissues, which regulates homeostasis by producing prostaglandins in the gastrointestinal mucosa, and by playing a role in platelet aggregation and renal blood flow. The COX-2 isoform is also constitutively expressed in a range of tissues and organs, including ovarian and renal tissues, but it is primarily induced by damage or tissue injury as a proinflammatory enzyme and is responsible for the production of various inflammatory mediators that amplify nociceptive input and transmission to the spinal cord (Lees *et al*., 2004). NSAIDs possess different levels of inhibition of the COX isoforms and for this reason may induce undesirable effects.

Adverse effects consist of gastric irritation and ulceration, development of protein-losing enteropathy, hepatic and renal damage, articular degradation, and prolonged bleeding time by prevention of platelet aggregation (Luna *et al*., 2007). These adverse effects are of the utmost importance in critical cases, especially when considering additional underlying disease processes, potential haemodynamic instability, and/or organ failure that may be present in this population of patients. A systematic review of NSAID-induced adverse effects in dogs has been published (Monteiro-Steagall *et al*., 2013).

NSAIDs should be administered with extreme caution to individuals with hypovolaemia, hypotension, pre-existing renal, hepatic and/or gastrointestinal disease, coagulation disorders and/or hypoproteinaemia. Indeed, NSAID toxicity is a common cause of gastrointestinal bleeding in the ICU that may require emergency intervention. On the other hand, patients may benefit greatly from NSAID therapy when a potential contraindication has been excluded. NSAIDs can be administered after the patient has been stabilized and once adequate renal function has been confirmed.

A panel of experts has provided guidelines for the use of NSAIDs in cats (Sparkes *et al*., 2010). In Europe, meloxicam is licensed for long-term use at 0.05 mg/kg/day in dogs and cats. Robenacoxib is also licensed for long-term administration in some countries. These guidelines are important because cats with maladaptive (chronic) pain will often benefit from NSAID therapy. This is also true for cats recovering in the ICU after a major surgical procedure.

Drug	Dose
Carprofen	Dogs: 4 or 4.4 mg/kg s.c., i.v., orally q24h for up to 4 days; oral dosing may be continued beyond 4 days; use lowest effective dose 2 or 2.2 mg/kg s.c., i.v., orally q12h for up to 4 days; oral dosing may be continued beyond 4 days; use lowest effective dose Cats: 2–4 mg/kg s.c., i.v. one dose only; do not follow-up with any additional doses
Cimicoxib	Dogs: 2 mg/kg orally q24h for 4–8 days; use lowest effective dose
Deracoxib	Dogs: 1–2 mg/kg orally q24h; use lowest effective dose 3–4 mg/kg orally q24h for up to 7 days
Firocoxib	Dogs: 5 mg/kg orally q24h for up to 3 days; use lowest effective dose
Ketoprofen	Dogs, cats: 1.0 mg/kg orally q24h for up to 3 days 2.0 mg/kg i.v., s.c., i.m. once postoperatively
Mavacoxib	Dogs: 2 mg/kg orally. Dose on day 0, day 14 and then once per month for up to a further 5 months
Meloxicam	Dogs: 0.2 mg/kg i.v., s.c. once followed by 0.1 mg/kg orally q24h 0.2 mg/kg orally once on day 1 followed by 0.1 mg/kg orally q24h; use lowest effective dose Cats: Up to 0.2 mg/kg s.c. once followed by 0.05 mg/kg orally q24h for up to 4 additional days 0.1 mg/kg orally once on day 1 followed by 0.05 mg/kg orally q24h; use lowest effective dose
Paracetamol (acetaminophen)	Dogs: 10–15 mg/kg orally q8–12h DO NOT USE IN CATS
Piroxicam	Dogs: 0.3 mg/kg orally q24h for two treatments, then q48h
Robenacoxib	Dogs: 1 mg/kg orally q24h; use lowest effective dose 2 mg/kg s.c. once followed by 1 mg/kg orally q24h Cats: 2 mg/kg s.c. once followed by 1 mg/kg orally q24h for a total of 6 days or as licensed
Tepoxalin	Dogs: 10 mg/kg orally q24h; use lowest effective dose
Tolfenamic acid	Dogs, cats: 4 mg/kg s.c., i.m. q24h for 3–5 days. Repeat once a week

21.23 Commonly used NSAIDs in the dog and cat.

Epidural analgesia

The advantages of the epidural route are proximity to the spinal cord receptors involved in the modulation and transmission of the noxious stimulus, and decreased systemic side effects. This characteristic may result in the ability to use lower doses, a longer duration of action, and fewer side effects compared with systemic administration of analgesics. Epidural technique is described elsewhere (*BSAVA Manual of Canine and Feline Anaesthesia and Analgesia*). In general, it is a safe procedure if performed after proper training using aseptic technique. In this chapter, the term epidural analgesia refers to the administration

of analgesics excluding local anaesthetics (epidural anaesthesia). A thorough review on the subject has been published (Steagall *et al*., 2017).

Epidural analgesia using opioids inhibits central sensitization and modulates afferent signals to the dorsal horn, reducing pain and analgesic requirements during the postoperative period, but does not impair motor tone or proprioception (Troncy *et al*., 2002). Contraindications include skin trauma and/or infection in the lumbosacral region, neurological diseases, coagulopathies and spinal cord trauma. The administration of preservative-free solutions to avoid neurotoxicixity is recommended. However, single epidural administration of morphine containing 0.1% sodium metabisulphite has been routinely used in dogs.

Clinical application:

- Lumbosacral epidural morphine (0.1 mg/kg diluted in 0.22 ml/kg of sterile saline) has been shown to be a good adjunctive analgesic technique in dogs and cats after thoracotomy or forelimb amputation. In cats, there is a risk of dura mater penetration during lumbosacral epidural injection. If this occurs, cerebrospinal fluid might be observed at the needle hub. In this case, preservative-free solutions must be injected using only one-third or one-half of the original volume to avoid excessive cranial spread of analgesic drugs and increased chance of adverse reactions.
- Epidural morphine should be used in combination with systemic analgesics and possibly loco-regional anaesthesia and NSAIDs (unless contraindicated).
- Epidural administration of (dex)medetomidine (3–6 μg/kg) produces profound antinociception and anaesthetic-sparing effects in dogs and cats. Systemic effects (i.e. sedation and negative cardiovascular effects) may occur. Its administration with bupivacaine is not recommended due to the possibility of prolonged motor blockade (15–18 hours).

An epidural catheter can be introduced into the lumbosacral space for intermittent or continuous administration of analgesics. Catheterization is usually accomplished aseptically using commercial kits (19, 20 and 24 G sizes) that include the catheter and a Tuohy needle, which has a curved bevel that facilitates direction of the catheter into the epidural space. Dislodgement, coiling and contamination of the catheter are the most common complications with this technique (Hansen, 2001). Clinicians should be familiar with epidural technique and anatomical landmarks before attempting epidural catheterization.

Local anaesthetics

Local anaesthetics block sodium and potassium channels in a reversible manner. They blunt peripheral nociceptive input and impulse conduction by blocking small unmyelinated C-fibres and myelinated Aδ fibres before other sensory and motor fibres (unmyelinated Aγ, Aβ and Aα).

Local anaesthetics are the most effective analgesics for the control of intraoperative pain when used at adequate doses and concentrations, and using proper anaesthetic techniques. They are used for loco-regional, intravenous regional, intra-articular, intrapleural, intraperitoneal, intratesticular, epidural, topical, transdermal (i.e. lidocaine patch and local anaesthetic cream) and infiltrative anaesthesia, peripheral nerve blocks (i.e. dental blocks), and/or as an adjuvant for GA (i.e. lidocaine infusion). Most of these techniques are readily used in clinical practice at low cost and with wide availability.

Local anaesthetics may cause toxicity after inadvertent intravenous administration or vascular absorption of an excessive dose. The initial signs of toxicity are CNS excitation, agitation and seizures, followed by CNS depression, coma, respiratory depression, cardiac collapse and death. Bupivacaine is an amide-type local anaesthetic with a prolonged effect (4–12 hours) which may induce ventricular arrhythmias and cardiotoxicity at lower doses than lidocaine. This is not a concern when maximum doses are respected (4 mg/kg for dogs and 2 mg/kg for cats every 4–6 hours) and careful technique is applied to avoid inadvertent intravenous administration.

Treatment of systemic toxicity involves administration of intravenous fluids, benzodiazepines and/or barbiturates, and if necessary endotracheal intubation followed by mechanical ventilation and oxygen therapy. Early treatment of cardiovascular toxic effects with administration of anticholinergics, vasopressors and antiarrhythmic drugs is also recommended. More recently, an intravenous lipid emulsion (4 ml/kg bolus, followed by 10 minutes of 0.5 ml/kg/min of Intralipid®) has been administered to reverse bupivacaine toxicity after cardiac arrest (Cave and Harvey, 2009) (see Chapter 19).

Wound infusion catheters: These devices have been used recently to prevent hyperalgesia and provide postoperative analgesia in dogs and cats after surgery. Complications are rare if appropriate technique is employed. These flexible indwelling catheters are embedded near the deep surgical wound; they are routinely used to deliver continuous or intermittent infusions of bupivacaine or ropivacaine postoperatively (Figure 21.24).

- Bupivacaine 0.5% is administered through the wound infusion catheter every 6 hours at 2 mg/kg in dogs and 1 mg/kg in cats. Alternatively, it can be given as a continuous infusion via the wound catheter at 0.3 mg/kg/h in the dog and 0.15 mg/kg/h in the cat. The total volume of bupivacaine can be diluted with sterile saline for better distribution, at a cost of potentially decreasing efficacy and duration of action.
- The injection of bupivacaine can be painful due to its low pH. The clinician may combine sodium bicarbonate 8.4% in the solution (1 ml to every 10 ml of bupivacaine) to reduce discomfort.
- Wound infusion catheters are available commercially in different sizes; however, they may be fashioned by using polyethylene tubing (Hansen, 2008).



21.24 Wound infusion catheter placed in a dog for the administration of local anaesthetic drugs in the postoperative period.

Intraperitoneal analgesia: Intraperitoneal administration of local anaesthetics (i.e. analgesia) reduces early postoperative analgesic requirements, pain scores, and time to first intervention analgesia after abdominal surgery in humans. Plasma concentrations of bupivacaine have been determined to be safe after intraperitoneal injection in cats (Benito *et al*., 2016a).

- Bupivacaine 0.5% (total 2 mg/kg) is splashed over the peritoneal space during laparotomy and/or near an area of abdominal tissue damage before laparotomy. The solution of bupivacaine can be diluted with an equal volume of sterile saline, resulting in a final concentration of 0.25%. The analgesic efficacy has been demonstrated in cats undergoing ovariohysterectomy (Benito *et al*., 2016b).
- The technique is normally performed in patients during surgery; however, it has been reported in dogs with pancreatitis and other abdominal conditions in the ICU. A catheter is introduced into the abdomen under adequate sedation and aseptic conditions. The skin can be desensitized with infiltrative or topical anaesthesia. Lacerations and organ perforation are potential complications.

Systemic administration of lidocaine: Lidocaine is an amide local anaesthetic that has been used as an adjunct to GA in dogs. This drug has been shown to have free radical scavenging, prokinetic, anti-arrhythmic and anti-inflammatory properties when injected systemically. It reduces the MAC of volatile anaesthetics in a dose-dependent manner, with minimal cardiovascular changes. Note bupivacaine should not be administered systemically because of serious cardiotoxic effects.

- Lidocaine can provide additional analgesia in dogs when administered by infusion (25–100 μg/kg/min i.v.) after a loading dose (1–2 mg/kg).
- The drug is added to the multimodal protocol to treat dogs that are refractory to conventional analgesics (i.e. opioids).
- For intraoperative usage, 300 mg of lidocaine is added to 1 litre of crystalloid solution and delivered at 10 ml/kg/h using a fluid pump. At this rate and concentration, the drug is given at 50 μg/kg/min.
- Lidocaine is not administered intravenously to cats due to its depressant cardiovascular effects in this species.

Epidural and loco-regional anaesthesia: A sacrococcygeal epidural block has recently been described to facilitate catheterization in male cats with urethral obstruction. The technique is performed under aseptic conditions and produces anaesthesia of the perineal area, penis, urethra, colon and anus (O'Hearn and Wright, 2011).

- The technique is preferably performed under sedation, although this may not be required if the cat is obtunded. Systemic administration of opioids alone (i.e. buprenorphine at 0.02 mg/kg i.m. or i.v.) or in combination with midazolam is recommended.
- Under aseptic conditions, the space between the sacrum and first coccygeal vertebra is palpated. The non-dominant index finger identifies the space. A 25 G 25 mm (1 inch) needle is used to penetrate the skin at midline at a 30–45 degree angle and advanced through the interarcuate ligament/ligamentum flavum.
- As the needle is advanced, there should be minimal resistance after entering the epidural space. The needle is repositioned if bone is encountered, or if blood is aspirated.
- The epidural space is identified (loss of resistance or a 'pop' sensation) and a syringe is attached. Preservative-free lidocaine 2% (0.1–0.2 ml/kg) is injected. Relaxation of the tail and perineal region is normally observed.

Lumbosacral epidural anaesthesia is not commonly used in critically ill dogs and cats with compromised/unstable cardiovascular function. Cardiac arrest due to excessive sympathetic blockade in dogs with uncorrected hypovolaemia has been reported. Hypovolaemia should be treated before epidural anaesthesia, with fluid therapy and appropriate treatment of hypotension.

Electrical nerve locators are devices used to facilitate peripheral nerve blockade (i.e. brachial plexus, sciatic and femoral nerve block). Clinical use of such equipment may improve accuracy and efficacy of a local block, and is an excellent tool to reduce intraoperative pain.

The advance of ultrasonographic imaging in emergency and critical care allows the clinician to perform ultrasound-guided nerve blocks, which have the potential advantage of reducing nerve injury, haematoma and/or accidental intravenous administration of local anaesthetics. For example, bupivacaine 0.5% was injected for ultrasound-guided pudendal nerve block (0.15 ml/kg for each site) in cats before perineal urethrostomy. This novel technique produced adequate pain relief when used in combination with buprenorphine (Adami *et al*., 2014).

Interpleural or intercostal anaesthesia: Bupivacaine 0.25–0.5% (1–2 mg/kg) is commonly administered via chest tubes or interpleural catheters to provide analgesia in conscious patients. The patient is restrained in lateral recumbency for approximately 10 minutes after injection, with its affected incision site towards the 'down side'. In this way, the drug is distributed close to tissues of interest, and has sufficient time for absorption. Systemic toxicity and complications are avoided using aseptic technique and adequate dosage regimens.

On the other hand, intercostal nerve blocks are used for postoperative pain after thoracotomy. In order to improve efficacy, this block is better applied during surgery when it is possible to directly visualize the nerve branches.

NMDA antagonists

There is now evidence that long-term changes in the CNS following peripheral tissue or nerve injury are dependent on the activation of NMDA receptors. Activation of NMDA receptors is involved with the transmission and exacerbation of nociceptive stimuli in the dorsal horn of the spinal cord, which plays a key role in neuropathic and chronic pain.

The role of the NMDA receptor in the processing of nociceptive input has led to renewed interest in NMDA receptor antagonists such as ketamine (Pozzi *et al*., 2006). NMDA antagonists may prevent central sensitization and the development of chronic pain. Doses of ketamine associated with NMDA antagonism are considered to be sub-anaesthetic and lower than those required for induction of anaesthesia.

Ketamine is used as an adjunctive analgesic agent in order to minimize the risk of central sensitization, potentially decreasing opioid requirements. Ketamine should be used as part of a multimodal analgesic approach and not as the sole method of providing pain relief in dogs and

cats after surgery. Ketamine infusions (see Figure 21.7) have been used for burns, refractory and neuropathic pain, and, following major surgery involving nerve resection (i.e. spinal surgery, sternotomy, thoracotomy, limb amputation), for excessive inflammation and patients with suspected hyperalgesia and allodynia. When combined with opioids and other analgesic techniques, ketamine infusion has been associated with analgesia of longer duration in dogs undergoing limb amputation (Wagner *et al*., 2002) and has an anaesthetic-sparing effect in dogs. Ketamine can safely be administered to critically ill patients. However, caution is recommended in cats with renal disease and impaired drug excretion. Sympathetic stimulation should be monitored.

Stimulation of NMDA receptors has been postulated to play a role in head trauma and tissue damage, and ketamine infusion has been proposed but not documented as a potential beneficial therapy in these cases. Respiratory function should be monitored to avoid hypercapnia, hypoventilation, hypoxaemia and consequent increases in cerebral perfusion pressure.

For intraoperative use, 120 mg of ketamine is added to 1 litre of crystalloid solution and delivered at 10 ml/kg/h using a fluid pump. At this rate and concentration, the drug is given at 10 μg/kg/min. Lidocaine and opioids (morphine) can be mixed in the same bag of fluids for multimodal analgesia.

Amantadine (3–5 mg/kg orally q12–24h) is also an NMDA receptor antagonist that has been administered to dogs with naturally occurring osteoarthritis refractory to NSAID therapy. Anecdotally, it has been used for maladaptive pain states.

Transdermal sustained-release formulations

Transdermal analgesia is used because of its convenience, while minimizing drug toxicity and providing analgesic efficacy. These types of drug delivery systems release a drug over an extended period of time in a sustained and controlled manner.

Transdermal patches (fentanyl, lidocaine and buprenorphine) are placed on the skin (Figure 21.25) to deliver a specific dose of drug through the skin and into the plasma.

The fentanyl patch ('off-label' administration) provides controlled release of the drug through a rate-limiting porous membrane with a drug reservoir. The dorsal neck or thorax is used for patch placement. The onset of action varies from 8–12 hours (cats) to 12–24 hours (dogs). Duration of action is expected to be around 72–96 hours. Fentanyl has shown great potential for postoperative analgesia in dogs, but variable plasma concentrations have limited its widespread application in cats (Hofmeister and Egger, 2004). The buprenorphine patch has not been tested in clinical trials, but data from an experimental study in the cat did not demonstrate antinociception.



21.25 Fentanyl patches placed on a dog.

The pharmacokinetics of lidocaine patches have been determined in dogs and cats. The lidocaine patch is 10 x 14 cm and contains 700 mg of lidocaine (50 mg of lidocaine per gram of adhesive patch) in an aqueous base with other inactive ingredients. This formulation of lidocaine produces analgesia without blocking sensory and motor input (Weil *et al*., 2007), and it can be used in cats. Systemic toxicity is usually not a concern since the formulation provides local analgesia without reaching significant plasma levels.

A sustained-release formulation of buprenorphine has been advocated to provide analgesia for up to 5 days in cats. However, there are no reports of the long-acting analgesic effects of this compound in veterinary medicine, and the pharmacokinetics and pharmacodynamics have not been reported.

A topical eutectic mixture of lidocaine and prilocaine (EMLA® cream) or a liposome-encapsulated formulation of lidocaine can be applied to the skin prior to catheterization and/or venepuncture in dogs and cats, in order to provide comfort and reduce stress during vascular catheterization. The cream is applied between 20 and 30 minutes before catheterization, and is covered with a bandage. The technique is helpful in critically ill patients where sedation is best avoided.

Alpha-2 adrenoreceptor agonists

The physiological and pharmacological effects of alpha-2 adrenoreceptors have been described above. Some critically ill patients might require a loading dose or infusion of dexmedetomidine or medetomidine to provide sedation and/or potentiate the analgesic effects of other classes of analgesics. A synergistic effect is expected when using a combination of opioids and alpha-2 agonists (i.e. infusion of dexmedetomidine and fentanyl).

This class of analgesic is best used in patients with normal cardiovascular function. Anecdotally, an infusion of dexmedetomidine has been administered after neurosurgery due to its neuroprotective effects. However, caution is recommended in head trauma patients as little is known about its effects on cerebral perfusion pressure and blood flow. On the other hand, appropriate treatment of pain may minimize increases in ICP in these cases by blunting the sympathetic response to noxious stimuli. A balance between analgesia and maintenance of homeostasis is the goal of therapy in these patients. A CRI allows rapid adjustment of sedative and analgesic levels. Dexmedetomidine at a 'micro-dose' of (0.25–0.5 μg/kg i.v.) can be a valid alternative for the treatment of dysphoria or emergence delirium caused by opioids, ketamine and inhalational anaesthetics. The specific alpha-2 adrenoreceptor antagonist atipamezole is used to reverse cardiovascular adverse effects, analgesia and sedation.

Tramadol

Tramadol is classified as a synthetic opioid-like substance with weak agonist effects at the μ opioid receptor (6000 times less than morphine) (Vettorato *et al*., 2010). Serotonin

and noradrenaline reuptake inhibition and their effect on the monoaminergic descending pain pathway mediate most of its analgesic effects. O-desmethyl-tramadol is the most important active metabolite produced by the liver's enzymatic degradation of tramadol; this active metabolite possesses 300–600 times the affinity for the mu (μ) opioid receptor as tramadol itself (Vettorato *et al*., 2010). Dogs may not produce this active metabolite in clinically relevant concentrations so the analgesic efficacy of tramadol has been questioned in this species. The suggested analgesic dose for dogs and cats is 2–5 mg/kg (i.v., i.m. and orally). The fact that tramadol is only available in an oral formulation dramatically limits its use in North America. However, it is widely used in parts of Europe and South America because of the availability of an injectable form, because it is not as strictly controlled as opioids, and because it has no relevant side effects. The only relevant reported side effect described in the human literature is serotonin syndrome if tramadol is administered in conjunction with other drugs that interfere with serotonin uptake (Indrawirawan and McAlees, 2014).

Gabapentin

Gabapentin is a calcium channel antagonist that can be used as an adjuvant in the treatment of hyperalgesia and allodynia. This drug has been widely used in the treatment of neuropathic pain in humans and rodents, although its mechanism of action is not fully elucidated. Anecdotally, gabapentin (5–20 mg/kg orally q8–12h) has been administered as part of a multimodal analgesic approach for the treatment of maladaptive (chronic) and neuropathic painful conditions. Sedation and lethargy are the two most common side effects. Further studies are needed to elucidate the role of gabapentin in small animal acute pain management.

Other therapies

The absence of evidence does not exclude the potential benefits of non-drug therapies in the treatment of pain. Physiotherapy and rehabilitation, therapeutic laser and heat, and (electro)acupuncture have been used alone or in combination with other analgesic therapies in dogs and cats. Physical therapy can be used to prevent and/or treat oedema and stiffening of joints and muscles in long-term patients in the ICU. Medical massage, cold (i.e. inflammatory states) and warm (i.e. muscle spasms) compresses are recommended where indicated.

There has been recent interest in the use of maropitant in the treatment of pain. The drug is administered to treat and prevent emesis in dogs by blocking NK-1 receptors in the chemoreceptor trigger zone in the CNS. There are reports of visceral analgesia after maropitant in mice and rabbits. However, maropitant has only been shown to reduce inhalant anaesthetic requirements in dogs, without any evidence of analgesic effect (Boscan *et al*., 2011).

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Useful websites

Association of Veterinary Anaesthetists:
https://ava.eu.com/wp-content/uploads/2015/11/AVA-Anaesthetic-Safety-Checklist-FINAL-UK-WEB-copy-2.pdf

Chapter 22

Nutritional support of the critical patient

Kathryn Michel

The provision of nutritional support to critical small animal patients is often postponed while the priorities of patient evaluation and stabilization are underway. However, studies in clinical patients and experimental animal models demonstrate the benefits of early nutritional intervention, which include enhanced immune function, wound repair and response to therapy, more rapid recovery time and improved survival (Heyland, 1998; Brunetto *et al*., 2010; Lui *et al*., 2012). Once major fluid and electrolyte deficits have been addressed and the patient is haemodynamically stable, the clinician should consider whether nutritional support is indicated as part of the patient's treatment programme. After all, the goal of supporting cardiopulmonary function and vascular perfusion is to ensure adequate tissue oxygenation. The reason tissues require oxygen is to generate energy efficiently from the metabolism of nutrients.

This chapter provides an overview of the potential benefits of nutritional support for the critical patient; demonstrates how to assess whether a patient should be considered a candidate for nutritional support; illustrates methods of providing nutrition to patients unable or unwilling to nourish themselves; and suggests methods for monitoring these patients to avoid or address complications.

Rationale for nutritional support

Any fasting animal must rely on its endogenous energy and nutrient stores until it is able to nourish itself again. A healthy animal deprived of food undergoes metabolic adaptations that improve its chances of survival by limiting the extent of tissue catabolism. The most critical of these adaptations are the ones that act to preserve endogenous proteins. Carbohydrate, fat and protein can all be utilized as sources of energy. Carbohydrate energy reserves are stored as glycogen in liver and muscle tissue, and fat is stored as triglycerides in adipose tissue. There are, however, no storage forms of protein. All endogenous proteins serve some functional purpose as structural proteins, enzymes, carrier proteins and so forth.

When an animal is deprived of food, glycogen is broken down to maintain blood glucose levels. Once the glycogen reserves have been depleted (within 24–48 hours) glucose must be synthesized from lactate, glycerol and certain amino acids in order to provide fuel for those tissues that preferentially or obligatorily use glucose for energy production. In the case of a simple fast in a healthy animal, metabolic adaptations over the course of days and weeks act to decrease tissue demands for glucose and thus spare amino acids.

Metabolic adaptations do not occur in the critical patient, however, even though these patients are often in a negative balance for both calories and nitrogen. The metabolic milieu of critical illness is very different from that of a simple fast. Mediators of the metabolic state (glucocorticoids, catecholamines, cytokines and other hormones) are released in response to tissue injury, infectious agents and inflammation. While some of the amino acids derived from the catabolism of endogenous proteins are either directly oxidized or converted to glucose, a significant portion are utilized for new protein synthesis. In the fasting critical patient it is not the lack of calories, but the lack of amino acids that is more likely to be life-threatening. Amino acids are necessary for the synthesis of vital host defence proteins such as immunoglobulins, clotting factors and acute phase reactants.

Providing an exogenous source of amino acids, calories and other nutrients does not eliminate this catabolic response, but can blunt it to some extent and act to support the patient's response to disease and injury while preserving endogenous tissues. Studies have confirmed that providing caloric intake can have a significant, positive effect on patient outcome (Remillard *et al*., 2001; Brunetto *et al*., 2010; Lui *et al*., 2012). An investigation in puppies with parvovirus showed that puppies receiving early nutritional intervention responded faster with improved gastrointestinal tract barrier function, and had shorter recovery times (Mohr *et al*., 2003). Unfortunately, despite this evidence, a negative energy balance is common in critical patients. Clearly, nutritional supplementation should be a part of any critically ill patient's strategic therapeutic plan. In patients that have already experienced a significant degree of malnutrition, nutritional support may be essential for survival.

Nutritional assessment: who and when to feed

With the greater availability of tubes, catheters and nutrient formulae specifically tailored to veterinary patients, providing nutrition, even to the most critically ill dog or cat, has become increasingly feasible. Careful patient selection is

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required, as nutritional support may have disadvantages. These can include an increased risk of morbidity and even mortality, prolongation of hospitalization and additional cost of treatment. It is therefore important to reserve the more aggressive forms of intervention, such as tube feeding or parenteral nutrition, for those patients where lack of nutrition will be most likely to have a negative impact on the clinical outcome.

Traditionally, the tests and techniques for nutritional assessment have been directed at the identification of malnourished patients. These include body condition scoring, assessment of weight loss, measurement of serum proteins, functional tests such as intradermal skin tests and sophisticated body composition analysis (e.g. dual X-ray absorptiometry, bioelectrical impedance). While the severely malnourished individual is easily identified, the diagnostic accuracy of these techniques remains unknown in less obvious cases, as there is no universally accepted 'gold standard' of malnutrition against which these tests can be compared.

A system of subjective evaluation of a patient's history and physical examination has been developed for use in humans and has been shown to be accurate in predicting which patients are at risk of developing nutrition-associated complications such as infections or poor wound healing. Whilst this technique has not been validated in veterinary patients, it is a straightforward approach, organizing easily available information, with the objective of classifying the patient's nutritional status as normal, marginal (slightly malnourished) or severely malnourished (Figure 22.1).

Medical history
• Changes in type of diet • Reduction in food intake on a voluntary and/or non-voluntary basis • Extent and time course of weight loss • Evidence of gastrointestinal disease • Effects of malnutrition on functional status • Underlying disease
Physical examination
• Wasting of muscle mass • Wasting of adipose tissue • Presence of oedema or ascites • Evidence of micronutrient deficiences • Ability to prehend, masticate and swallow normally • Evidence of physical trauma, in particular facial injuries
Evaluation of current intake
• Calorie count • Estimation of caloric needs

22.1 Nutritional assessment.

Taking the history

A medical history should always include specific questions about the patient's diet and feeding behaviour. It is important to find out whether the current diet and food intake are normal or have changed. Particular attention should be paid to recent reductions in intake on both a voluntary and involuntary basis. Weight loss should be evaluated with respect to its extent and the duration of time over which it has occurred. Loss of a particular amount of body mass over a 2 week period may be far more significant than the same loss over a 2 month period, since a greater proportion of the loss is likely to be lean tissue. Evidence of chronic gastrointestinal disease should be noted, as disorders causing malassimilation of dietary nutrients can lead to both protein-calorie malnutrition and specific micronutrient deficiencies, depending on the condition. A history may also reveal information about the impact of malnutrition on functional status, as revealed by weakness and exercise intolerance. Finally, knowledge of the underlying disease process helps to indicate whether continued deterioration or restoration of nutritional status is to be anticipated.

The physical examination

Several systems for scoring canine and feline body condition have been published. None of these systems is ideal for evaluation of the hospitalized patient, since they do not reflect the alterations in body composition seen in the acutely critical animal. As previously discussed, the critical patient is often in a state of accelerated catabolism, and lean tissue wasting outstrips adipose tissue breakdown in these circumstances. A more appropriate approach is to evaluate caloric and protein 'reserves' separately, by assessing adipose tissue and skeletal muscle mass, respectively. Muscle condition score systems have been developed that can be used in conjunction with a conventional body condition score to better characterize critical patients (Michel *et al*., 2004; Michel *et al*., 2011).

In addition to assessment of body condition, other features of the physical examination that may indicate a state of malnutrition include oedema, ascites and skin or hair coat lesions that are specific for micronutrient deficiencies.

Selection of patients for nutritional support

Once a patient has been classified as being normal, mildly malnourished or obviously malnourished, it is necessary to decide whether that patient is a candidate for nutritional support (Figure 22.2). At this point, it is essential to have an accurate assessment of the patient's food intake. In cases where the patient appears to have a diminished appetite but is still voluntarily consuming food, it may be necessary to measure food intake for a day or two in order to determine if consumption is adequate. This assessment method requires the estimation of an 'ideal' caloric intake for the patient. Methods for the calculation of energy requirements of hospitalized patients will be discussed in the next section. Ideally, the patient should be consuming a diet balanced for all its nutritional needs. Often, palatable table foods are substituted for pet foods when animals are ill. If the patient refuses to take in at least 50% of its calories in the form of a pet food for more than a few days, efforts should be made to ensure that essential nutrients, such as protein and water-soluble vitamins, are being adequately supplied.

For the patient in which estimated food intake falls short of its goal (see the section on energy requirements below), it must be decided whether the lack of optimal nutrition will have an impact on clinical outcome. This is not always an easy judgement. Some general guidelines are listed in Figure 22.2. Patients assessed as obviously

• Patients that were significantly malnourished before the onset of their current illness • Patients that are anticipated to be NPO (nil by mouth) for more than 3–5 days • Previously well nourished patients that develop or are likely to develop serious complications (e.g. septic peritonitis, open discharging skin wounds, aspiration pneumonia)

22.2 Selection of patients for nutritional support.

malnourished and that have a serious illness should be considered automatic candidates for nutritional support if their voluntary food intake is below estimated goals. Normal or mildly malnourished critical patients, however, can also be at risk of malnutrition-associated complications, since their nutritional status can deteriorate rapidly in the face of suboptimal intake. It has been established that patients have a better clinical outcome when nutritional support is initiated early on in their illness. The art of nutritional assessment is therefore to select patients that are likely to have a severe and complicated clinical course and prolonged partial or total anorexia. Furthermore, nutritional support should be initiated as soon as is clinically feasible.

Nutritional requirements of critical patients

Energy requirements

The daily energy requirement of an individual reflects the energy required for basic life processes (often referred to as resting energy requirement or RER), a small amount of energy used for the assimilation of nutrients, a variable amount of energy expended for body temperature regulation and the energy expended in physical activity. Generally, the more unwell the patient, the more likely it is that RER will approximate that patient's total energy expenditure. It was previously believed that energy expenditure was often significantly elevated in critical illness, possibly to twice what would be expected under normal circumstances. This was the rationale for the IER (illness energy requirement) approach to estimating the energy requirements of hospitalized patients. That method involved multiplying RER by 'illness factors' ranging from 1.1 to 2.0. Clinical experience and measurements of the energy expenditure of actual patients using indirect calorimetry suggest that the energy expenditure of the majority of critical patients, both human and veterinary, is at most only modestly elevated above RER (Chan, 2004). In addition, feeding excessive calories to critical patients may cause a number of untoward effects, including gastrointestinal problems, electrolyte disturbances, hyperglycaemia, hepatic dysfunction and respiratory distress.

Consequently, the current recommendation for estimation of the caloric requirements of critical veterinary patients is to use one of the formulae for RER (Figure 22.3). The use of RER as a caloric goal is a reasonable and safe starting point, for both patients whose voluntary food intake is being assessed and for patients that will be nutritionally supported. The amount fed to a given patient can always be increased if that patient experiences weight loss.

Interspecific formulae	Feline formula
RER = 70 (Wt_{kg})$^{0.75}$ RER = 30 (Wt_{kg}) + 70	RER = 40 (Wt_{kg})

22.3 Calculation of resting energy requirement (RER) for dogs and cats. The interspecific formulae tend to overestimate feline energy requirements.

Protein requirements

While it appears that most hospitalized patients do not have RERs that differ greatly from normal, their protein requirements can be significantly greater during critical illness. The amount of protein an animal requires in its diet is a reflection of amino acid needs for protein synthesis and replacement of degraded or lost amino acids. Cats also have an obligatory need for amino acids for energy production. The nature of the protein source will also affect the amount required in the diet, since some protein sources are limiting in one or more essential amino acids.

Ideally, the dietary source of protein for critical patients should be highly digestible and contain all of the essential amino acids in appropriate amounts. As a rule, animal sources of protein, in particular egg and milk proteins, meet these criteria. For patients receiving enteral nutrition, protein should comprise at least 20–30% of calories (2–3 g/kg bodyweight) for dogs and >30% of calories (3 g/kg bodyweight) for cats. There are veterinary products designed for the enteral nutritional support of veterinary patients that meet these guidelines (Figures 22.4 and 22.5).

Some critical patients with renal or hepatic dysfunction may not tolerate this quantity of protein. These patients do not have decreased protein requirements; rather, they have impaired ability to eliminate nitrogen byproducts of protein metabolism (e.g. urea and ammonia). Therefore, feeding strategies for these patients should involve supportive therapies that improve the elimination of protein metabolic waste products (i.e. fluid diuresis for renal failure, oral lactulose for hepatic failure), thus allowing as much protein intake as possible.

Characteristics	Recovery RS	a/d	Purina
Energy density	1 kcal/ml	1.2 kcal/ml	1.6 kcal/ml
Protein	37%	33%	28%
Fat	59%	55%	63%
Carbohydrate	4%	12%	9%
Tube suitability	>8 Fr	>8 Fr	>8 Fr
Manufacturer	Royal Canin	Hill's Pet Nutrition, Inc.	Iams Company

22.4 Tube feeding diets for cats and dogs. Note that the energy is given on an 'as fed' basis; protein, fat and carbohydrate are given on an 'energy' basis. Other products are available in different countries and veterinary professionals should ensure they are aware of product availability within their local market. The chracteristics in this figure are as described for the product in the USA.

Characteristics	Feline and canine liquid convalescence support
Energy	1.1 kcal/ml
Protein	37%
Fat	47%
Carbohydrate	16%
Tube suitability	All types
Manufacturer	Royal Canin

22.5 Liquid diets for cats and dogs. Note that the energy is given on an 'as fed' basis; protein, fat and carbohydrate are given on an 'energy' basis. Other products are available in different countries and veterinary professionals should ensure they are aware of product availability within their local market. The chracteristics in this figure are as described for the product in the USA.

Micronutrient requirements

In addition to water, calories and protein there are at least 25 other essential nutrients, including fatty acids, minerals and vitamins. The effect of critical illness on a patient's micronutrient requirements is unknown. Current recommendations are to provide amounts that meet at least normal adult maintenance requirements (Figure 22.6). Many patients have adequate endogenous stores of most of these nutrients to survive weeks or in some cases months of reduced food intake. A number of these nutrients, in

Nutrient	Units/1000 kcal ME	Adult Dog		Adult Cat	
		Minimum	*Maximum*	*Minimum*	*Maximum*
Protein	g	45		65	
Arginine	g	1.28		2.6	
Taurine	g			0.5	
Linoleic acid	g	2.8		1.4	
Arachidonic acid	g			0.05	
Phosphorus	g	1.0	4.0	1.25	
Potassium	g	1.5		1.5	
Zinc	mg	20		18.8	
Vitamin A	IU	1250	62,500	833	83,325
Vitamin D	IU	125	750	70	7520
Vitamin E	IU	12.5		10	
Thiamin (vitamin B1)	mg	0.56		1.4	
Riboflavin (vitamin B2)	mg	1.3		1.0	
Pantothenic acid	mg	3.0		1.44	
Niacin (vitamin B3)	mg	3.4		15	
Pyridoxine (vitamin B6)	mg	0.38		1.0	
Folic acid	mg	0.054		0.2	
Cobalamin (vitamin B12)	mg	0.007		0.005	

22.6 Micronutrient requirements of dogs and cats, according to the Association of American Feed Control Officials nutrition profiles. ME = metabolizable energy.

particular the water-soluble vitamins, are, however, very labile, and patients may become significantly depleted in a short period of time. Therefore, depending on a patient's nutritional status at the time of presentation, it may already be suffering from deficiencies of one or more B vitamins or electrolytes.

Most veterinary enteral products are nutritionally balanced, so, barring problems with nutrient assimilation, deficiency states should not arise. Electrolyte deficiencies are generally secondary to excessive fluid losses as opposed to malnutrition, and are addressed in Chapter 5. In the case of severe protein-calorie malnutrition or accelerated catabolism due to critical illness, extreme imbalances of potassium, phosphorus and magnesium may occur. This situation, known as 'refeeding syndrome', will be discussed in more detail in the section on complications of nutritional support.

In recent years there has been a good deal of investigation into the benefits of supplementation of specific nutrients such as glutamine, arginine, omega-3 fatty acids and zinc in critically ill human patients. A review of these nutrients is beyond the scope of this text; however, it is important to recognize that clinical trials in human patients have not consistently demonstrated benefits from their use. Moreover, there is virtually no research on the safety and efficacy of these nutrients in critical small animal patients. Hence, the evidence is currently not strong enough to make specific recommendations for the supplementation of these substances beyond ensuring that intake is sufficient to meet essential requirements.

Routes of nutritional support

Enteral nutrition

The age-old adage 'if the gut works, use it' still holds true. The intestinal epithelium requires glutamine and regular access to nutrients to maintain the health of enterocytes (including the height of the villi and the function of brush border enzymes) and to support other neuroendocrine exchanges between the pancreas, stomach and small intestine. The nourishment provided via enteral feeding, therefore, helps to protect against bacterial translocation, absorption of endotoxin and the development of sepsis in critically ill patients unwilling or unable to maintain their own nutrient intake. Fortunately, the enteral route is also more economical, easier to implement and associated with fewer complications than parenteral feeding. Methods of enteral feeding include coaxed feeding, chemical stimulation of appetite, and infusion of nutrients via feeding tubes within the gastrointestinal tract, bypassing the oral cavity (Figure 22.7). Deciding which method to use is dependent upon several factors, including the animal's current nutritional status and general state of health, the estimated length of time that nutritional support will be required, the animal's tolerance of general anaesthesia, the experience of the clinician and the associated costs of the procedures.

Coaxed feeding

Coaxed feeding, depending on the patient, may be an easily applied method of nutritional support adequate for the hyporexic patient. This method is directed at encouraging voluntary intake and does not imply force feeding. Force feeding should be avoided, as it increases the stress of an already compromised patient, increases the likelihood of aspiration and injury, and more commonly results in the topical, rather than enteral, application of nutrients. Force feeding may also induce or reinforce the development of a learned food aversion in the patient, which hinders further voluntary intake. Gently tempting the patient with small, frequent meals of a highly palatable diet consisting of wet, odoriferous, warm food in a quiet environment may stimulate self-feeding. Home-prepared chicken, fish or red meats are often successful food choices. If the patient does not voluntarily eat what is offered, gently syringing a soft or liquid diet into the corner

Method	Advantages	Disadvantages
Coaxed feeding	Simple, potentially less stressful	Not effective in many animals May induce learned food aversion
Chemical stimulants	Simple, 'reminds' patients of the taste of foods	Short term (2–3 days) Side effects depending on drug
Naso-oesophageal tube (Cats: 3.5–5 Fr) (Dogs: 3.5–8 Fr)	Easy to place, least invasive, low cost Requires minimal sedation, if any Use up to 1 week	Not well tolerated by some patients Must use an Elizabethan collar Requires liquid diet
Oesophagostomy tube (8–18 Fr)	No special equipment required Can be used long term	Requires brief general anaesthesia for placement Infection of stoma may occur
Gastrostomy tube (14–30 Fr)	Easy to maintain Can be used long term	Requires general anaesthesia for placement Specialized equipment needed Tube must remain in place for a minimum of 14 days
Enterostomy tube (5–8 Fr)	Bypasses pancreas and dysfunctional gastrointestinal tract	Requires general anaesthesia for placement Liquid diet constantly infused Requires intensive care Tube must remain in place for a minimum of 14 days

22.7 Routes of enteral nutritional support.

of the mouth may stimulate the animal to eat on its own. If the animal does not express an interest in eating on its own after the first one or two attempts at coaxed feeding, other options should be considered.

Chemical stimulation of appetite

If adequate intake is not attained, chemical stimulants have been reported to increase the appetite and 'remind' a patient of the taste of food, encouraging them to eat voluntarily. Application of these drugs may result in the consumption of 25% of the daily requirement in responsive cats (Figure 22.8). However, this option is not without a degree of risk and should be reserved as a short-term 'kick-start' in patients likely to recover in a short time period rather than an option for the long-term anorexic or inappetent patient. The side effects of benzodiazepine appetite stimulants may include drowsiness, excessive sedation or, more seriously, idiosyncratic hepatic necrosis in cats (following oral administration of diazepam), limiting their usefulness. Mirtazapine and cyproheptadine have fewer known side effects (although cyproheptadine can cause excitement/agitation) and may be more effective choices as appetite stimulants. When using appetite stimulants, it is important that the animal's clinical response is accurately and honestly recorded with an ongoing assessment of calorie intake.

Drug	Dose	Side effects
Diazepam	0.05–0.15 mg/kg i.v., i.m. or 1 mg orally q24h	Sedation, idiosyncratic hepatic necrosis
Cyproheptadine	8 mg/m^2 or 2–4 mg/cat orally q12–24h 0.2 mg/kg orally q24h (dogs)	Excitability, aggression, vomiting
Mirtazipine	1.9 mg/cat orally q24–72h 3.75–7.5 mg/dog orally q24h	Serotonin antagonist; should not be administered to patients receiving MAO inhibitors

22.8 Chemical stimulation of appetite. MAO = monoamine oxidase.

Tube feeding

In many critically ill animals, the best way to ensure that adequate nutritional intake is achieved is to place a feeding tube and deliver food and water according to the calculated requirements. Several types of feeding tubes have been described and will be reviewed here. In general, the more proximal the feeding tube, the more physiologically appropriate the feeding regimen and the less likelihood that a gastrointestinal upset will occur. The author prefers the use of naso-oesophageal tubes for the short-term feeding of critically ill patients, and oesophagostomy or percutaneously placed gastrostomy tubes for periods longer than 7 days.

Naso-oesophageal tubes: These are the simplest, least invasive and most commonly used feeding tubes and are excellent choices for the short-term feeding of hospitalized patients. Owners will rarely opt to maintain these tubes in the home environment, but it can be done. Soft flexible polyvinyl feeding tubes are easily placed into the nostril with a topical anaesthetic and minimal sedation (Figures 22.9 and 22.10). They should terminate just short of the lower oesophageal sphincter rather than in the stomach, to avoid inducing gastro-oesophageal reflux. The largest tube diameter that fits snugly in the internal nares should be used to maximize the feeding capacity. Correct tube placement should be confirmed by radiographs. Naso-oesophageal feeding tubes are contraindicated in patients that have rhinitis or severe facial trauma involving the nares and nasal turbinates, those



22.9 Placement of a nasogastric tube in a 5-month-old dog. A 5 Fr naso-oesophageal tube has been measured to the 9th rib space and marked with a piece of white tape, and a topical anaesthetic has been placed in the left nostril. To facilitate passage into the ventromedial nasal meatus, the nares are directed upwards.

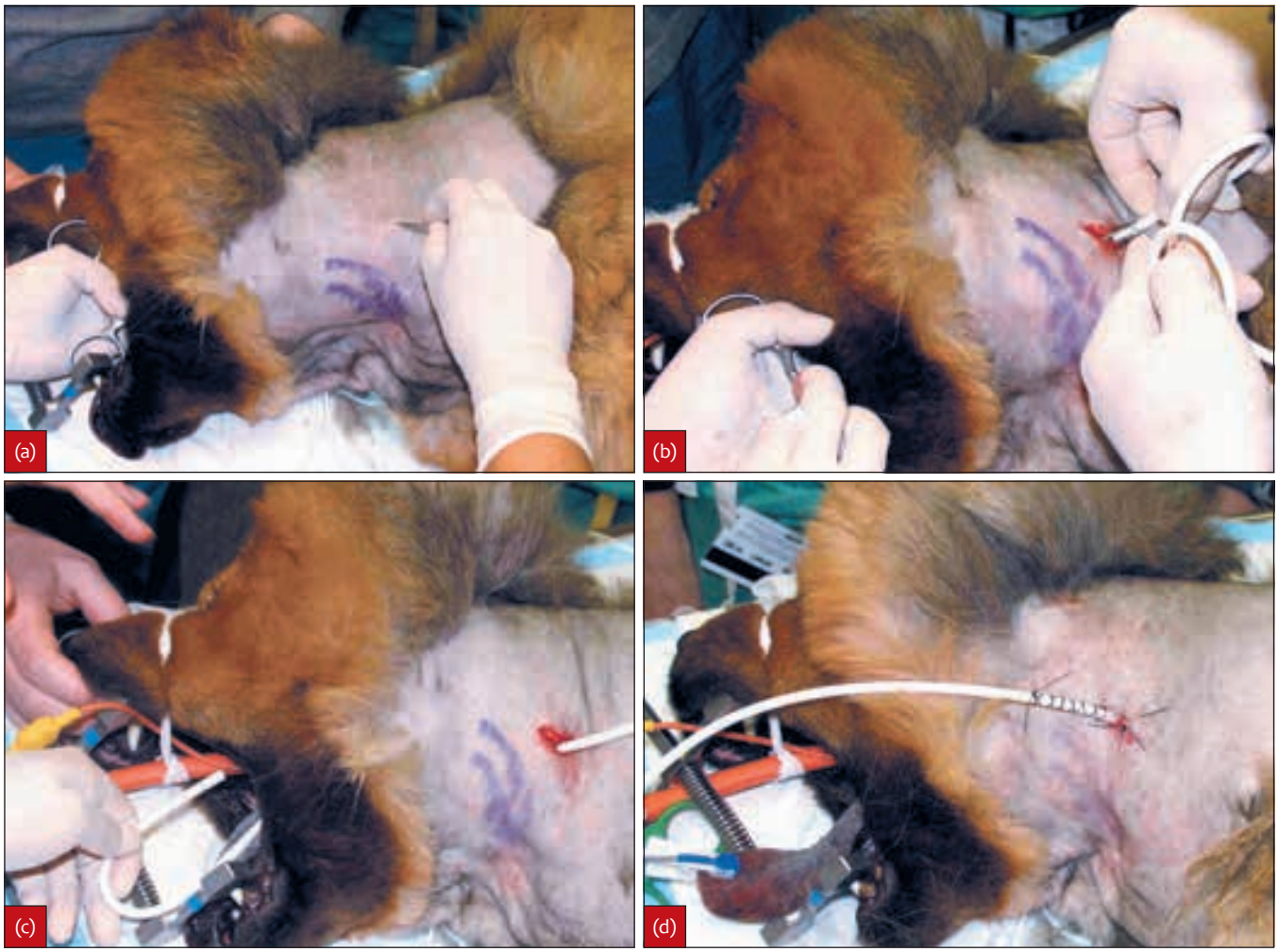


22.10 German Shepherd Dog with a naso-oesophageal tube. Once in place, the tube is secured to the external nares with 'superglue', or preferably a small suture passed retrograde through a 24 G needle. Two more sutures secure the tube to the dorsum of the nose and the top of the head, out of the dog's direct line of vision. An Elizabethan collar prevents the dog from interfering with the tube.

that are experiencing protracted vomiting and/or regurgitation, those that are semi-conscious or unconscious, and those that have physical or functional abnormalities of the pharynx, larynx or oesophagus.

Once in place, these tubes may be used intermittently, dividing the total daily intake into small frequent meals or, less commonly, a liquid diet may be given as a continuous infusion. Complications that can arise with the use of these tubes may include rhinitis, vomiting or regurgitation. Aspiration of oesophageal contents is more likely if the animal is very weak or suffering neurological deficits and is fed in, or remains in, prolonged lateral recumbency.

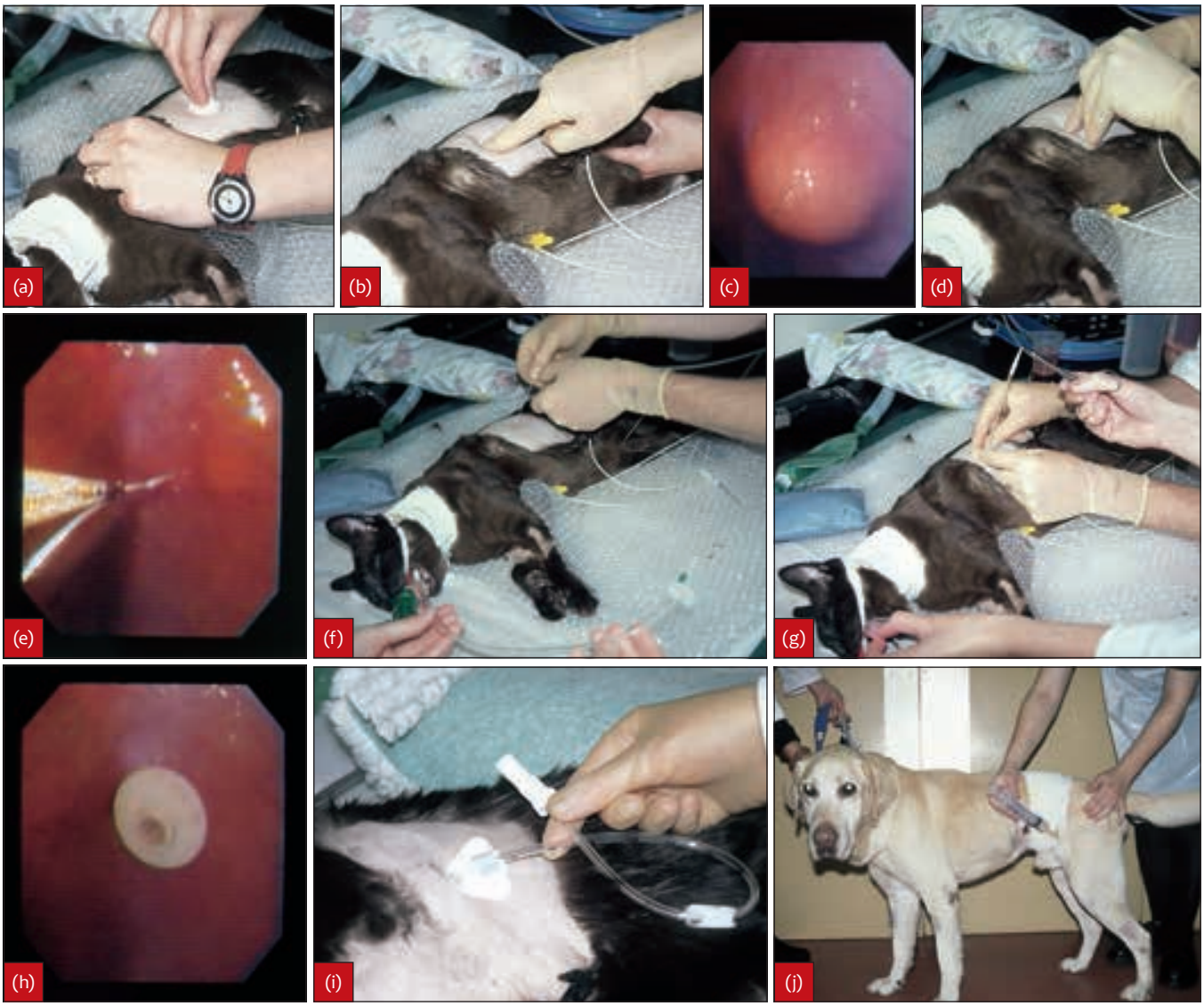
Oesophagostomy tubes: Oesophagostomy tubes are variably sized tubes that are easily placed under light anaesthesia with minimal equipment requirements. Large-bore oesophagostomy tubes may be an ideal option for the general practice environment, as they are relatively simple to place and can be maintained and used for months. The only major associated complication is the development of infection at the entry site, therefore meticulous care of the surgical wound is essential to maintain the tube. For this reason, oesophagostomy tubes are the preferred mode of support and pharyngostomy tubes, which have higher complication rates, are no longer recommended. Placement of an oesophagostomy tube is shown in Figure 22.11. Patients can be fed orally while oesophagostomy tubes are in place. Once the patient is reliably consuming its daily caloric needs voluntarily, the tube can be removed by cutting the suture and pulling the tube out smoothly in an orad direction; the wound is left to heal by second intention.



22.11 Oesophagostomy tube placement. (a) Forceps have been placed in the cervical oesophagus and their points are being used as a guide for the position of the skin incision. (b) The forceps are forced outwards through the incision to the external surface. The feeding tube is grasped with the forceps and drawn into the pharynx through the oesophagostomy incision. (c) The tube is redirected down the oesophagus. (d) The oesophagostomy tube in its final position. It should be capped off and sutured in place and the neck bandaged.

Gastrostomy tubes: Gastrostomy tubes have become invaluable for the long-term nutritional support of critically ill or recovering patients. Gastric feeding tubes may be placed surgically, endoscopically or by a 'blind' placement technique. Surgical placement of gastric feeding tubes is convenient when abdominal surgery is warranted for other purposes such as performing organ biopsies or removal of masses. These tubes may be 'pexyed' in position and tightly sealed with omentum to prevent leakage. Balloon-tipped Foley catheters designed for use in the urinary tract should be avoided owing to the possibility of balloon rupture and displacement of the catheter, increasing the risk of peritoneal cavity contamination.

An easier and less invasive means of gastric tube placement is by use of an endoscope (Figure 22.12). Tubes may be placed efficiently within 10–15 minutes under general anaesthesia, the limiting factors being accessibility of and experience with the endoscopic equipment. The most economical type of feeding tube is fashioned from a mushroom-tipped catheter in which only minor alterations are needed. The tip can be removed to add a feeding conduit and the widened catheter end is then cut to form two



22.12 Gastrostomy tube placement. (a) Under general anaesthesia, the cat is placed in right lateral recumbency and an area (~10 cm x 10 cm) just behind the ribcage is clipped and surgically prepared. A mouth gag is used to protect the teeth from damaging the endoscope. The stomach is insufflated with air to move all other abdominal contents, specifically the intestines and spleen, away from the body wall. (b) The site within the stomach where the tube will be anchored is chosen with the aid of an assistant, who wears sterile gloves and indents the surface of the prepared skin just caudal to the rib cage and directed cranially. (c) This indentation can be seen by the endoscopist, who then directs the assistant to an area well away from the pyloric outflow tract into the fundus of the stomach where the tube is to be situated. (d) A small (~2 mm) incision is made in the skin just over the site and a 19 G catheter (dogs and cats) is sharply introduced. (e) The catheter stylet is removed and a piece of suture material is passed into the stomach. Biopsy forceps are used to retrieve the end of the suture material, which is pulled into the endoscope as it is removed from the patient. The assistant must allow the suture material to thread easily into the stomach, and the catheter can then be removed. (f) The suture material now passes into the stomach via the body wall, extends up the oesophagus and out of the mouth. Human enteral feeding tubes such as this one (Fresenius), have a narrow tip to pass through the body wall. When using a mushroom-tipped pezzar catheter, a small pipette tip is placed on to the end of the suture material (tip threaded first), and the suture material is then fixed to the tube with multiple knots. (g) The assistant slowly retracts the suture material, exiting the body wall until the tip of the pipette can be palpated. The stomach is held in place while the tube is pulled through the gastric mucosa and exits the body wall. A haemostat clamp can be used to grab hold of the pipette tip and exert an even upward pressure. Simply pulling the suture material may result in breakage. (h) Once the tube has been pulled into place, it is important to go back and look in the stomach to verify that the tip is not stuck at the lower oesophageal sphincter and the tube is in an appropriate position, away from the pyloric outflow tract. (i) Flexible plastic fittings hold the feeding tube in place. Tight placement may result in pressure necrosis and increase the incidence of infection. The tube site is then wrapped in sterile material. (j) A percutaneously placed gastric tube in a 3- year-old Labrador with megaoesophagus.

stents, which are placed on either side of the positioned tube to anchor the tube in place and to prevent its inadvertent removal (Figure 22.13). Once placed, the tube should be left in place for a minimum of 14 days prior to removal to allow a seal to form between the stomach and the abdominal wall. The benefit of using this type of tube is that when the animal no longer requires nutritional support, the tube is simply pulled firmly and the stents slip off, allowing complete removal of the tube. The internal stent is usually small enough to be passed in the faeces and rarely if ever requires a second anaesthetic for endoscopic retrieval. The disadvantage of these tubes is that they may be inadvertently removed by a strong tug and so must remain carefully wrapped when not in use.



22.13 A relatively inexpensive feeding tube can be made from a mushroom-tipped catheter with minor alterations. The wide end of the catheter is cut to form two stents, which are placed on either side of the body wall (internal stent shown) to anchor the tube in place and to prevent its inadvertent removal.
(Reproduced from Battaglia (2006) with permission from Elsevier)

A simpler, yet more expensive, system is the use of pre-packaged enteral feeding tubes. The author currently uses a commercially available 16 or 20 Fr polyurethane tube (MILA International). The advantages of these kits are that they contain all that is necessary to place the tube and they are suitable for use in cats and small to medium dogs. In large dogs, the internal bumper is not large enough to secure these tubes in place, and it is necessary to use the technique using a mushroom-tipped catheter as described above.

'Blind' tube placement, without direct visualization of the site of internal insertion, is facilitated by the use of a long, rigid stylet passed through the mouth into the oesophagus and palpated through the stomach wall (Torrance, 1996). This may be a useful technique in the hands of some experienced practitioners when endoscopic or surgical placement is not possible; however, given the potential complications, the author recommends oesophagostomy tube placement instead in most cases. Care must be taken not to lacerate the spleen or oesophagus during placement, and it is advisable to verify tube placement radiographically following the procedure.

Gastric feeding tubes may be used for periods of up to 1 year if carefully maintained (Figure 22.14). Most patients tolerate the tubes quite well, although body wraps are advised to prevent the stoma site from becoming soiled. In the overly enthusiastic patient, an Elizabethan collar may be necessary to prevent chewing or removal of the tube. Fortunately, complications are uncommon, but can include splenic laceration during placement as discussed above, infection or cellulitis at the site of exit from the body wall, vomiting due to slippage of the tube back into the gastric lumen, or peritonitis from contamination of the peritoneal cavity.

1. Do not use the tube for the first 24 hours. This will allow a primary seal to form between the stomach and body wall.
2. Start with small amounts of water, 5 ml/kg, to flush the tube.
3. Feed only one-half of the calculated daily caloric requirement the first day. This is divided into small (20–30 ml) frequent (5–6) feedings.
4. Warm the food to body temperature and inject into the stomach over several minutes. If the animal begins to retch or swallow, slow down or stop altogether and try again at the next feeding.
5. Aspirate the contents of the stomach with an empty syringe prior to each feeding. If gastric emptying is delayed and there is more than half the previous meal in the stomach, skip the feeding and consider motility modifiers such as metoclopramide.
6. **Always follow basic tube etiquette:** flush before and after feedings with 5–10 ml of water, to clear debris and maintain tube patency.
7. On the second day of use, increase the feeding to the calculated caloric intake if tolerated.
8. Change sterile bandages every 2–3 days after initial placement, check placement of the tube and clean the wound.

22.14 General guidelines for the use of gastrostomy tubes.

Low-profile enterostomy 'button' devices, which occupy the fistula between the gastrointestinal tract and the body wall, currently used in human medicine, are available for use in veterinary patients and may be left in place long term with minimal complications.

Enterostomy tubes: Placement of feeding tubes beyond the stomach is rarely indicated, but in cases of pancreatitis, diffuse gastric mucosal disease, protracted vomiting or delayed gastric emptying, an enterostomy tube may be essential. Enterostomy tubes are most commonly placed surgically, or they may be introduced nasally or through a gastric tube and then directed through the pylorus with an endoscope or fluoroscopy. At surgery, a flexible, small-bore tube is threaded into the proximal jejunum or distal duodenum and secured with a purse-string suture. The delivery end exits through an abdominal stab incision and is fixed to the abdominal wall (Simpson and Elwood, 1994). Feeding through an enterostomy tube must be carefully controlled since the diets are often concentrated in order to supply enough calories, and therefore may cause osmotic overload and diarrhoea. As with gastrostomy tubes, enterostomy tubes must remain in place for a minimum of 14 days to allow a seal to form with the abdominal wall. Continuous infusion of a dilute liquid diet is the preferred method of use, therefore the patient must remain hospitalized while the tube is in place, which limits its long-term employment.

Parenteral nutrition

Parenteral nutrition (PN) is nutrition delivered by the intravenous route. It can be life-saving for patients who cannot tolerate enteral feeding. However, because there are numerous drawbacks associated with this form of nutrition, it should be reserved for patients with no other feeding option, and for whom the need for nourishment is felt to be a critical factor in their recovery. Generally, these are patients for whom enteral feeding is contraindicated or hazardous.

Special solutions are used for intravenous feeding; they must be mixed aseptically and in a specific order. PN is best delivered continuously (although this is not absolutely necessary), therefore 24-hour nursing care is desirable. In addition, since many of the potential complications of PN (sepsis and various electrolyte disturbances) can be life-threatening, careful monitoring of the patient is mandatory.

Therefore, a significantly higher cost of care is an expected consequence of the intensive care and special supplies required to deliver PN to a patient.

Venous access

Ideally, a catheter should be dedicated for PN infusion alone, because of the increased risk of catheter sepsis associated with the infusion of a nutrient-rich solution. By dedicating a line to PN and observing strict aseptic care of the line and its connections, the potential for bacterial contamination is reduced. Central venous access is preferable to peripheral access, since PN solutions are hyperosmolar and associated with the development of thrombophlebitis. However, PN solutions can be diluted adequately to permit peripheral infusion as long as the patient is not at risk of fluid volume overload. PN solutions infused via peripheral catheters should not exceed 800 mOsm/l and if possible should be less than 600 mOsm/l. In addition, use of fine-bore polyurethane or silicone elastomer cannulae will greatly reduce the risk of thrombophlebitis.

Parenteral nutrition solutions

Basic PN is composed of a protein source (crystalline amino acid solution), a carbohydrate source (dextrose) and a fat source (lipid emulsion). Vitamins, electrolytes and trace minerals can also be added so that the resulting solution is complete and balanced, at least according to standards for healthy dogs and cats.

Because most veterinary patients receive PN for limited periods of time (often a week or less), the focus should be on providing protein, calories and the more labile vitamins (water-soluble vitamins). Electrolyte supplementation is managed as a component of fluid therapy rather than as part of PN. Providing more complete nutrition to a patient parenterally is problematic due to compatibility problems between various nutrients and nutrient formulations, as well as expense. If the patient is not on a balanced enteral diet within a week of starting PN, fat-soluble vitamins are supplemented separately (intramuscularly or subcutaneously) on a weekly basis. The water-soluble vitamin folate should also be supplemented separately in long-term PN patients, as it is omitted from parenteral B-complex preparations. Parenteral trace mineral supplements are also available for use in these patients.

The service of a pharmacy at a human hospital or home transfusion service can be utilized for obtaining PN solutions. If PN solutions are to be made in house, they should be made fresh daily and must be mixed in a specific order under aseptic conditions. Special PN compounding bags can be used, or solutions can be prepared in evacuated glass containers. In general, amino acid and dextrose solutions are mixed first and then electrolyte and mineral solutions are added. Great care must be taken when adding combinations of electrolytes, especially phosphorus and calcium, because precipitates can easily form. Next, multivitamins are added, and finally the lipid emulsion. The lipid emulsion is fragile and the suspended triglyceride particles can coalesce or even precipitate. Precipitation of lipid emulsions can be detected by visual inspection after the solution has been sitting for a while. There should not be any indication of separation or layering of the final solution. Risk of fat embolization can be eliminated by using an infusion set that contains a 1.2 μm filter to deliver PN solutions containing lipids.

Prescription formulation

Figure 22.15 shows a worksheet and a sample calculation for formulating PN. Because of the limited discussion of PN in this chapter the reader is encouraged to seek a more detailed review of this technique. There are several guidelines for formulating PN for small animals in the literature (Hill, 1994; Chan, 2005).

Day 1 goal: 50% RER Day 2 goal: 100% RER
(see Figure 22.3 for RER formulae)

Protein calories:
Dogs: 15–25% of RER; Cats: 25–35% of RER
Select % protein calories based on the patient's protein status and ability to tolerate dietary protein.

Non-protein calories:
30–70% from lipid
30–70% from dextrose
Dogs: provide 50% of non-protein calories from lipid and 50% from dextrose unless there is pre-existing hyperlipidaemia or hyperglycaemia.

Cats: provide 70% of non-protein calories from lipid and 30% from dextrose unless there is pre-existing hyperlipidaemia or hyperglycaemia. Cats are more likely to become hyperglycaemic, which is why more calories are provided as lipids as a rule.

Solutions:

1. Amino acids
   - 1 g of amino acids provides approximately 4 kcal
   - Use solutions containing 3.5–5% amino acids (350–500 mOsm/l)
   - Use solutions without additional electrolytes to simplify management of electrolytes with fluid therapy
2. Dextrose
   - 10% dextrose contains 500 mOsm/l and provides 0.34 kcal/ml
   - 20% dextrose contains 1000 mOsm/l and provides 0.68 kcal/ml
3. Lipid emulsions
   - Use 20% lipid emulsions, which contain 268–340 mOsm/l and provide 2 kcal/ml
4. Phosphorus
   - Use standard parenteral potassium phosphate solutions
5. B vitamins
   - Use standard parenteral B complex solutions

Example calculations: a 17.5 kg dog without hypoproteinaemia

RER = $70(17.5)^{0.75}$ = 600 kcal/day
Goal calories for day 1 = 0.5(600) = 300 kcal

1. **Amino acids**
   (0.15)(300 kcal) = 45 kcal from protein
   45 kcal ÷ 4 kcal/g = 11.25 g
   4.25% amino acid solution = 0.0425 g protein/ml, therefore you need 265 ml of a 4.25% amino acid solution (x ml = 11.25 g ÷ 0.0425 g/ml)
2. **Non-protein calories**
   (0.85) (300 kcal) = 255 kcal from lipid and dextrose
   a. 20% lipid emulsion to provide 50% non-protein calories = 127.5 kcal
      20% lipid emulsion = 2.0 kcal/ml, therefore you need 64 ml of a 20% lipid emulsion (x ml = 127.5 kcal ÷ 2.0 kcal/ml)
   b. 20% dextrose to provide 50% non-protein calories = 127.5 kcal
      20% dextrose solution = 0.68 kcal/ml, therefore you need 188 ml of a 20% dextrose solution (x ml = 127.5 kcal ÷ 0.68 kcal/ml)
3. **Potassium phosphate**
   Dosed at 8mM/1000 kcal delivered, therefore you need 2.4 mM of a potassium phosphate solution (x mM = (8 mM)(300 kcal) ÷ (1000 kcal))
4. **Vitamin B complex**
   Dosed at approximately 2 ml/l infused.
   Total infused for day 1 = 518 ml, therefore 1.0 ml B complex should be sufficient
5. **Infusion rate**
   518 ml/24 hours = 22 ml/h
   The osmolarity of this solution is approximately 625 mOsm/l

Day 2 calculations:
Same as for day 1, but substitute 600 kcal for 300 kcal.

22.15 Worksheet for peripheral parenteral nutrition. RER = resting energy requirement.

Monitoring and treating the complications of nutritional support

The monitoring required in critically ill patients receiving nutritional support is typically no different from the minimum expected for any critical patient: routine physical examinations; body temperature; heart rate and respiratory rate; twice daily weight measurements; and assessment of hydration status and general demeanour. Laboratory values frequently assessed include total protein, albumin, packed cell volume, blood glucose, gross inspection of plasma for lipaemia, serum electrolytes and blood urea nitrogen. Alterations in these parameters may indicate improved patient status due to correction and support of the underlying disease or, conversely, may signal early warnings of complications associated with nutritional support. In a study of anorexic cats, high creatine kinase (CK) activity was found, exceeding an average of 250 times that of normally nourished cats (Fascetti *et al*., 1997). In response to nutritional intervention, the CK activity decreased and eventually returned to normal. CK may prove to be a useful marker of nutritional status in the clinical setting.

Complications associated with enteral nutrition fall into the categories of mechanical, gastrointestinal or metabolic. Mechanical complications most commonly encountered include obstruction of the feeding tube, dislodgement of a tube, or infection/cellulitis at the tube entry site. Obstruction of feeding tubes may be minimized by the use of foodstuffs of the appropriate consistency in relation to the tube size. Tubes of 5 Fr diameter and smaller should only ever admit liquid diets, whereas larger-sized tubes may admit thoroughly liquidized canned food diets, but still risk blockage if the diets are not properly diluted and the tubes are not flushed after feeding. Ideally, to minimize the chances of blockage and to prevent wear, tubes should be used solely for feeding purposes and not for the administration of medications. If a tube becomes obstructed, radiographs may be indicated to confirm whether the tube is kinked rather than clogged. Should a tube become clogged and unresponsive to hydrostatic pressure, cola or, alternatively, pancreatic enzyme powder mixed in sodium bicarbonate can be left in the tube for 5–10 minutes to help dissolve the offending material. If neither is successful, the tube requires replacement.

Gastrointestinal complications are, unfortunately, common in animals receiving enteral nutritional support, and typically manifest as nausea, vomiting and diarrhoea. These may be avoided by a slow introduction to feeding and by administering dilute solutions to avoid sudden intraluminal hypertonicity. The first day of feeding should begin with incremental amounts of water and half of the daily caloric requirements divided into five or six feedings. If feeding is tolerated well, the full calculated daily caloric requirements are given on the second day. Prior to each feeding via a gastrostomy tube, the tube is aspirated to ensure that the stomach has emptied from the previous meal (with normal gastric motility, gastric residuals should be <20 ml and consist primarily of secretions as opposed to food). If not, the amount remaining may be subtracted from the current feeding. Despite these precautions, diarrhoea may occur due to villous atrophy of prolonged anorexia, intolerance of the chosen diet, antibiotic-induced alterations in intestinal flora, or as a manifestation of the underlying illness. Treatment with motility-modifying drugs, the addition of fibre or a change to PN may be necessary.

Metabolic derangements resulting from enteral nutritional support are rare. The duration of illness and the severity and nature of the underlying disease may predispose some patients to glucose intolerance (and hence hyperglycaemia or glucosuria), hyperlipidaemia or electrolyte disturbances. These derangements are more commonly encountered in patients receiving PN. Correction of these abnormalities requires manipulation of the fluid regimen and dietary components, and appropriate therapy for the underlying disorder. Persistent hyperglycaemia may infrequently require the use of insulin. A phenomenon known as 'refeeding syndrome' has been described in which, upon initiation of nutritional support to malnourished patients, severe metabolic derangements occur, the most significant of which is hypophosphataemia. In one review, refeeding resulted in hypophosphataemia and haemolysis in cats within 12–72 hours (Justin and Hohenhous, 1995). Cats with diabetes mellitus or those with high liver enzyme activities, hyperbilirubinaemia and weight loss seem to be at increased risk. These patients should be closely monitored for the development of low serum phosphorus and subsequent haemolytic anaemia when initiating nutritional support (Justin and Hohenhous, 1995).

Complications of PN are more common than those of enteral support and are associated with the mechanics of administration, sepsis or metabolic derangements, the occurrence of which depends upon the components and proportions administered. Mechanical complications are frequent and include broken, chewed, obstructed or dislodged administration lines and catheters. They rarely have an effect on the patient, but do increase the possibility of sepsis. PN should be supplied via dedicated fluid lines to centrally placed catheters, the meticulous care of which are essential. To avoid contamination and potential sepsis, the ports must be tightly secured and wrapped with disinfectant-soaked swabs. The site of catheter placement should be inspected daily, gently scrubbed and wrapped aseptically. Patients receiving PN should be closely monitored for the development of fever, depression and leucocytosis, which signal probable sepsis. When these signs are recognized, the catheter is removed, the tip is cultured and aggressive fluid and, if necessary, broad-spectrum antibiotic therapy is instituted.

Metabolic derangements occur frequently in patients receiving PN but rarely result in clinical signs. Common abnormalities include hyperglycaemia, glucosuria, azotaemia, lipaemia and electrolyte changes, such as hypokalaemia, hypomagnesaemia and hypophosphataemia. Cats and some dogs readily develop glucose intolerance and may require short-term insulin therapy. Azotaemia and lipaemia are likely to be a result of highly concentrated intravenous infusions of amino acids and lipid emulsions, which overwhelm the body's capacity for utilization or storage. Electrolyte disturbances occur most frequently in patients that are vomiting and are easily addressed with appropriate fluid therapy. Refeeding syndrome, manifested by hypophosphataemia and haemolysis (see above), is more common in patients receiving PN than in those managed with enteral nutritional support.

The key to minimizing metabolic abnormalities is early detection. Frequent haematological and biochemical profiles are indicated to allow prompt correction of fluid electrolyte concentrations. In addition, antiemetics should be administered, infusion rates adjusted and proportions of components modified.

Conclusion

Nutritional support is rapidly and appropriately becoming a primary concern rather than an afterthought for our critically ill veterinary patients. As we become more experienced in the application of nutrition, we are increasingly aware of its benefits in shortening recovery time and decreasing morbidity and mortality experienced by our patients. The time and effort required for stabilization of the critical patient is well spent if we do not allow that patient's nutritional status to become a limiting factor in its recovery.

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Chapter 23

Bacterial infections in the critical patient

Iain Keir and Dawn Merton-Boothe

Antibacterial therapy is among the most important and commonly used therapeutic interventions in the critical patient. However, critically ill patients are also among those at greatest risk for development of antibacterial resistance. Invasive procedures, immunosuppression, polypharmacy and other factors increase this risk. Furthermore, there is an increasing concern in society regarding overuse of antibacterial therapies and a duty for all veterinary surgeons (veterinarians) to ensure they are used responsibly.

The use of antibacterials in emergency and critical care poses unique challenges. Timeliness of administration often necessitates implementation of therapy prior to receipt of culture and susceptibility data. Changes in drug disposition associated with disease complicate design of effective and safe dosing regimens. Nonetheless, the appropriate implementation of antimicrobial therapy is essential. Rapid diagnosis of infection in the absence of culture and susceptibility data, appropriate empirical antibacterial selection based upon knowledge of likely pathogens and their potential resistance, and avoiding the adverse effects of these medications are paramount. The principles that should guide antibacterial selection and therapy in the critical care patient are listed in Figure 23.1.

1. Therapy should be timely: a 10% increase in mortality might be anticipated for each hour's delay in the implementation of appropriate antimicrobial therapy.
2. Therapy should be implemented after obtaining an appropriately collected culture sample.
3. Appropriate therapy should target any potential bacteria infecting the patient, including nosocomial organisms. As such, the spectrum should be broad and target potentially resistant microbes.
4. De-escalation to lower tier drugs should be implemented as soon as possible.
5. In general, bacteriostatic drugs should be avoided.
6. In general, combination therapy might be implemented in the patient infected by or at risk of developing resistant microbes.

23.1 Key points for consideration when treating critically ill patients with antibacterials.

Diagnosing infections

The first step in the appropriate use of antibacterials is to determine if an infection that requires systemic antimicrobial therapy is present. A complete physical examination will help determine the likelihood and potential location of infection. However, clinical signs do not confirm infection but rather the presence of inflammation, which can also result from non-infectious disease processes.

An attentive physical examination will also indicate whether a once-localized infection is resulting in systemic sequelae referred to as sepsis. Sepsis is defined in dogs and cats as an infection (bacterial, fungal or viral) causing alterations in heart rate, respiratory rate, temperature and white blood cell count (Dickinson *et al*., 2015). If sepsis is suspected or identified, the urgency of the investigation and treatment provided to the patient needs to be increased in order to prevent detrimental sequelae to organ dysfunction, and an associated increased risk of patient mortality.

If signs of systemic inflammation have been identified, the location of the suspected infection should be determined based upon the physical examination, i.e. thoracic *versus* abdominal, or other locations such as bite or burn wounds. Regarding the thoracic cavity, pulmonary infections may be associated with tachypnoea and pulmonary crackles on auscultation, while pleural space infections are associated with tachypnoea and absence of lung sounds ventrally on auscultation. In contrast, abdominal infections (peritonitis) are associated with abdominal pain, and renal inflammation may be associated with pain on palpation of the kidneys. Once the location of the problem has been identified, the clinician is then in a position to perform further diagnostic investigations in a timely and focused manner, prior to the administration of antibacterials.

The importance of diagnosing the presence of bacterial infection prior to the administration of antibacterials cannot be overemphasized. If the clinician cannot find supporting evidence of an infection, the patient is unlikely to need antibacterials, and therefore short- and long-term adverse effects of antibacterials can be avoided and the risk of resistance reduced. In addition, the owner will not incur the cost of unnecessary medication. Furthermore, once the site of any infection has been identified, every effort must be made to collect a sample from the infected site for culture and susceptibility testing to guide future antibacterial selection. The administration of antibacterials prior to sample collection can result in misleading microbiological results, including a failure to culture bacteria from the sample. However, the knowledge that many critical patients have already been treated with antibiotics should not deter collection and testing of samples, as this category of patient has a high risk of infection with resistant bacteria. Documentation of susceptibility can be vital to direct therapy in these patients. Obtaining an adequate sample will also allow in-house cytology to be performed, which can rapidly confirm the presence or absence of inflammation and infection.

The method used to obtain a sample of the infected tissue will depend upon the organ system involved and the stability of the patient. While all efforts should be made to obtain an appropriate sample, this should not be pursued to the detriment of the patient. It is also important that samples are collected and handled in a sterile manner, including aseptic preparation of sample sites and use of sterile gloves.

Diagnosis and sample collection

Pneumonia

Once a clinical and radiographic diagnosis of bacterial pneumonia is suspected (see Chapter 7), there are various options for obtaining a sample from the lungs for culture and susceptibility testing, each of which has its own distinct advantages and disadvantages (Figure 23.2).

Technique	Advantages	Disadvantages
Transtracheal wash	Minimal sedation required Reduced risk of oropharyngeal contamination	Risk of skin contamination Non-selective sample collection Technically challenging in small patients Low diagnostic yield Contraindicated in the presence of severe dyspnoea or coagulopathy
Endotracheal wash	High diagnostic yield Short/light anaesthesia compared with bronchoalveolar lavage	Risk of oropharyngeal contamination Anaesthesia still required Non-selective sample collection
Bronchoalveolar lavage	Selective sample collection Minimal risk of upper respiratory tract/ oropharyngeal contamination High diagnostic yield	Requires deep anaesthesia Temporary reduction in lung function after procedure Can induce transient hypoxia
Transcutaneous pulmonary aspirate	Light sedation and/or local anaesthesia required Selective sample collection	Very low diagnostic yield Risk of lung laceration Risk of pneumothorax

23.2 Methods of sampling from the lower respiratory tract.

Pyothorax

Although more commonly occurring in cats, pyothorax can also occur in dogs (see Chapter 7). Ultrasonography of the thoracic cavity can be used to confirm the presence of fluid within the pleural space, and is preferred to thoracic radiographs because it can be performed with the patient in a sternal position without sedation, and is therefore less stressful for the patient.

To determine the nature of the pleural fluid and confirm the presence of bacterial infection, thoracocentesis must be performed. This procedure often serves as both a diagnostic and a therapeutic tool in these patients.

Bacterial peritonitis

Rapid identification of patients with bacterial peritonitis is an essential skill in emergency and critical care medicine (see Chapters 11 and 12). Typically, dogs will present with a history of acute vomiting and inappetence and will have clinical signs attributable to sepsis (tachycardia, tachypnoea, pyrexia/hypothermia, leucopenia/leucocytosis) with some degree of abdominal pain. In cats, the signs of bacterial peritonitis can be less obvious, with a more protracted disease course, infrequent signs of abdominal pain (38%) or vomiting (42%), and non-specific signs that include lethargy and anorexia (Babyak and Sharp, 2016).

When bacterial peritonitis is suspected or even when it is a possibility, simple steps can be performed rapidly to rule it in or out. It is important to provide cardiovascular support while diagnostic investigations are being performed:

- Perform a brief abdominal ultrasound examination (abdominal focused assessment using sonography for trauma (aFAST) (see Chapter 1)
  - Identify the presence of free abdominal fluid
- If ultrasonography is not available, abdominal radiography should be performed before abdominocentesis
  - Peritoneal effusions will result in a lack of abdominal serosal detail
  - Free gas within the abdomen is usually associated with a ruptured viscus and a high risk of bacterial peritonitis
- Perform abdominocentesis
  - Ultrasound-guided or four-quadrant technique
  - On rare occasions a diagnostic peritoneal lavage (DPL) may be required
- Perform in-house cytology on the free abdominal fluid
  - Presence of intracellular bacteria confirms the diagnosis of bacterial peritonitis
  - Presence of high nucleated cell count may be strongly suggestive of peritonitis, even if bacteria are not identified cytologically
- As bacterial peritonitis is a surgical emergency, an in-house cytological examination of the fluid is essential.

Once free abdominal fluid has been identified, the next step is to obtain a sample in a sterile fashion. Ultrasound-guided abdominocentesis is recommended as this minimizes the risk of contamination from inadvertent enterocentesis. The technique is best performed using a 25–40 mm (1–1½ inch) 21 G needle attached to a 5 ml syringe with the patient in lateral recumbency. The area of interest is clipped and prepared aseptically and the needle is slowly guided into the pocket of fluid by ultrasonography, then gentle suction is applied to collect the sample.

If ultrasound-guided abdominocentesis cannot be performed, a four-quadrant abdominocentesis should be undertaken. For this technique, the skin over the abdomen is clipped and aseptically prepared, extending from 5 cm cranial to the umbilicus to the pubis, and 5 cm on both sides of the midline. Needle-only abdominocentesis is performed 2–3 cm cranial and caudal to the umbilicus, on both the left and right side. It is helpful to have the needle in place for 60 seconds and to gently rotate the needle to encourage fluid flow. Fluid may drip from the needle or collect within the needle hub; either way each sample site should be evaluated independently.

Initial fluid collection may be unsuccessful if only a small amount of fluid is present. Repeating the aFAST/abdominocentesis once the patient has received adequate intravascular volume expansion may allow retrieval of a sample as more fluid accumulates; however, this may cause unnecessary delays in both diagnosis and treatment. Alternatively, a DPL may be performed.

To perform a DPL the abdomen is prepared as for a four-quadrant abdominocentesis. A 60–140 mm (2½ to 5½ inch) 16 G over-the-needle catheter is used. Before insertion, 3–4 fenestrations are created in the distal third of the catheter using a sterile scalpel blade. 1–2 ml of lidocaine is injected at the site of catheter insertion, usually 2–3 cm caudal and lateral to the umbilicus. To aid passage of the catheter, a small stab incision can be made through the skin only. The catheter is inserted into the peritoneal cavity and the authors typically direct in a caudodorsal direction towards the urinary bladder. Once the catheter is in place and the stylet has been removed, 20 ml/kg of warm saline is infused through the catheter, then a sterile injection cap is placed over the catheter. The patient is then gently rolled from one lateral position to another to help re-distribute the fluid, taking care not to dislodge the catheter. The final step is to collect a fluid sample from the catheter that has remained *in situ* by applying gentle suction via a syringe or by gravity flow into a sterile collection system. If the catheter does become dislodged then ultrasound-guided or four-quadrant abdominocentesis may be used to retrieve fluid as described above. Frequently, much less fluid is retrieved than was infused, as fluid can be rapidly absorbed across the peritoneal membrane.

Urinary tract infection

The clinical signs and management of bacterial urinary tract infections are summarized in Chapter 8.

Cystocentesis is considered the gold standard when sampling urine for bacterial culture and susceptibility as it minimizes the risk of contamination from the urethra. However, this may not be practical in patients that have recently voided urine and have a small bladder size, when ultrasonography is not available, or when a coagulopathy is present. In these situations, collecting a sample via sterile catheterization of the urinary bladder is recommended.

Occasionally, for example in the presence of a ureteral obstruction, it is necessary to obtain a sample from the renal pelvis by performing ultrasound-guided pyelocentesis.

Supporting evidence on a standard urinanalysis for the presence of a urinary tract infection includes the presence of blood and protein in the urine on a urine dipstick. Clinicians should avoid relying on the urine dipstick to determine the presence of leucocytes within the urine and always confirm positive results by urine sediment examination. A urinary sediment examination can be performed quickly and easily in-house to provide a rapid result, with indications of a urinary tract infection including the presence of numerous leucocytes and bacteria.

Cytology and analysis of fluid samples

Diagnosis of a bacterial infection in emergency cases relies on good quality in-house cytological examination, which can only be done with good staining technique and a good quality microscope. The fluid sample for cytology should be collected into EDTA, which preserves cell morphology. In-house staining is most commonly performed with rapid Romanowsky stains (e.g. Diff-Quik®) following the manufacturer's recommendations for staining technique and maintenance of the solutions.

The number of nucleated cells in fluid samples should be counted and reported as cells per microlitre, providing useful information for diagnosis of a bacterial infection. Septic effusions are expected to have high neutrophil counts, with evidence of immature neutrophils possibly with cytoplasmic degenerate changes. Bacteria are not always seen.

To confirm the presence of a bacterial infection causing pneumonia or peritonitis, the bacteria must be present within the cytoplasm of the leucocytes. It must be remembered, however, that bacteria may not be visualized within a sample on cytology, but may still be grown on culture. However, the presence of extracellular bacteria could indicate contamination, such as enterocentesis in the case of peritonitis or oropharyngeal contamination in the case of pneumonia. In fluid samples collected from other sites the presence of intra- or extracellular bacteria provides confirmation of a pathogenic infection.

To improve the presurgical accuracy of a diagnosis of septic peritonitis, point-of-care biomarkers have been assessed. Specifically, the comparison of lactate and glucose values in the fluid with those values in a concurrently obtained plasma sample has been suggested as a way to increase the confidence of a positive diagnosis of abdominal sepsis. In this case, fluid lactate above that of plasma accompanied by fluid glucose lower than that of plasma supports a diagnosis of septic peritonitis. The results should be interpreted with some caution and the understanding that the consumption of glucose and production of lactate within the peritoneal effusion is most likely a product of the white blood cells in the effusion and not specifically bacteria.

Development and prevention of antimicrobial resistance

Bacteria acquire resistance through two major mechanisms: reduction of their exposure to antimicrobials, or alteration of antimicrobial target sites. Reduction of their exposure to antimicrobials is accomplished by the constitutive presence or induction of inactivating enzymes, decreased expression of membrane porins, or increased expression and activity of membrane efflux pumps.

Of these, the former, perhaps best represented by beta-lactamases, generally results in resistance that is restricted to within the same class of antimicrobial. Among the beta-lactamases, extended-spectrum beta-lactamases (ESBLs) are particularly problematic. Expressed in response to exposure to third-generation cephalosporins, these enzymes may not be detected by susceptibility testing unless specifically tested for. More problematic is that these enzymes target all third-generation cephalosporins, including higher-tier drugs with an extended spectrum towards Gram-negative isolates. Resistance associated with destructive enzymes is generally shared through mobile genetic elements, such as plasmids. Resistance can develop rapidly among different organisms, but removal of the drug often removes selection pressure for resistance.

In contrast to destructive enzymes, resistance mediated by porins or efflux pumps generally demonstrates broad substrate specificity and thus confers multidrug resistance. Among the classes of drugs, resistance to fluorinated quinolones is notable because after several steps, high-level, multidrug resistance emerges as a result of increased efflux pump activity. Changes in target proteins often result from spontaneous mutations, and as such develop more slowly. Others, for example, meticillin-resistant *Staphylococcus* spp., reflect acquisition of a gene which codes for an altered penicillin-binding protein, rendering the isolate resistant to all beta-lactams. Resistance due to mutations of target proteins is also generally only relevant within that antimicrobial class.

In its 2013 report, the US Centers for Disease Control indicated that the greatest risk or contributor to antimicrobial resistance is antimicrobial use. Further, in human hospitals, antimicrobial therapy is considered inappropriate in up to 50% of patients (US Department of Health and Human Services, 2013).

Two primary approaches might be employed to reduce antibacterial resistance in hospitals: reduction of the dissemination of antibacterial-resistant bacteria; and decrease specific processes that promote antibacterial resistance (Figure 23.3). The authors recommend a 'three Ds' approach to reducing antimicrobial resistance:

Primary approach	Method
Reduce dissemination of antibacterial-resistant bacteria	• Wash hands and wear gloves when handling all patients • Use strict isolation precautions in high-risk patients • Promote active culture surveillance to identify patients with antibacterial-resistant bacteria • Use aseptic technique for invasive procedures • Prescribe appropriate initial antibacterial therapy • Disinfect commonly used instruments, patient care material, and the environment • Develop local protocols and guidelines for infection control; monitor compliance
Decrease specific processes that promote antibacterial resistance	• Decrease unnecessary use of antibacterials • Avoid prophylactic use of antibacterials, unless in high-risk patients (e.g. neutropenia) • Hit 'hard' with initial therapy and de-escalate to narrow spectrum when possible based on culture results or patient response • Use dosing regimens designed to kill the entire infecting inoculum • Avoid antibacterial homogeneity, i.e repeated use of select antibacterials for all patients; consider antibacterial rotation or mixed use of classes • Develop and promote the use of guidelines for optimizing antibacterial use

23.3 Practical methods to reduce and prevent antibacterial resistance.

- De-escalate antimicrobial use
- Design the dosing regimen such that a residual resistant inoculum is less likely to remain in the patient ('dead bugs do not mutate')
- Decontaminate the environment.

De-escalation of antibacterial use can be approached using several tactics. Perhaps the most important is to avoid use of systemic antibacterial therapy if equally effective alternatives exist. In the critical patient, this approach should be used cautiously due to the unstable, and sometimes life-threatening, state of the patient. For this environment, de-escalation might more prudently focus on a 'get in quick, hit hard, and get out quick' approach. Antibacterial therapy should be initiated with the best drug for the patient, one that is likely to be effective against any potential infecting microbe, including nosocomial infections if appropriate for the hospital. This generally involves a third- or fourth-tier antimicrobial.

Factors that determine the 'tier' assigned to any drug may vary. The authors propose that drugs defined as belonging to higher tiers are those in which:

- The spectrum includes organisms generally resistant to lower-tier drugs
- There are safety concerns for the patient
- Drugs for which resistance, in the event of therapeutic failure, is likely to be multidrug resistant
- Drugs that are important to human medicine (Figure 23.4).

The authors do not ascribe to policies that preclude the use of antimicrobials considered important to human medicine. Rather, use of the lowest tier, but best drug for the patient is recommended. Once the decision is made to use an antimicrobial, the clinician should commit to designing a dosing regimen that minimizes resistance. This means choosing the most appropriate drug as well as designing its dose. Therapy should be rapidly de-escalated if the patient responds, limiting length of treatment to less than 7 days or if culture data indicate that a lower-tier drug might be implemented.

Antibacterial class, tier and mechanism	Key members	Characteristics	General spectrum	Comments
• Beta-lactams; aminopenicillins • 1st tier • Cell wall inhibitor	Amoxicillin, co-omoxiclav Ampicillin, ampicillin/sulbactam	Weak acid, water-soluble, bactericidal, time-dependent	Gram-positive, Gram-negative, anaerobes	Short half-life (approximately 1 h). Not a good first choice drug unless patient is confirmed not exposed to antimicrobials
• Beta-lactams; extended-spectrum penicillins • 3rd tier • Cell wall inhibitor	Ticarcillin (with clavulanic acid) Piperacillin (with tazobactam) Carbenicillin	As above	As above, plus extended Gram-negative spectrum	Short half-life (approximately 1 h). Beta-lactamase susceptible: combine with beta-lactamase inhibitor
• Beta-lactams; carbapenem • 3rd or 4th tier • Cell wall inhibitor	Imipenem Meropenem	As above	As above	Short half-life (approximately 1 h); largely beta-lactamase resistant but may be susceptible to extended-spectrum beta-lactamases (carbapenemases)
• Beta-lactams; 1st-generation cephalosporin • 1st tier • Cell wall inhibitor	Cefalexin Cefazolin	As above	Cefalexin: *Staphylococcus* Cefazolin – Gram-positive (*Enterococcus* is resistant) and some Gram-negative	3 to 5 h half-life

23.4 Summary of antimicrobials used in critical care, based on chemistry–structure activity relationship (class). (continues) ▶

Antibacterial class, tier and mechanism	Key members	Characteristics	General spectrum	Comments
• Beta-lactams; 2nd-generation cephalosporin • 3rd tier • Cell wall inhibitor	Cefoxitin Cefuroxime	As above	As for cefazolin; plus anaerobes	Short half-life (approximately 1 h), not susceptible to extended-spectrum beta-lactamases
• Beta-lactams; 3rd-generation cephalosporin • 2nd to 3rd tier • Cell wall inhibitor	Cefovecin Cefpodoxime Ceftiofur Ceftazidime Cefotaxime	As above	Varies markedly. Some include *Pseudomonas* spp. Use should be based on culture and sensitivity testing	Markedly variable half-life. Induce and susceptible to extended-spectrum beta-lactamases
• Aminoglycosides • 3rd or 4th tier • Ribosomal inhibitor	Gentamicin Amikacin	Weak base, water-soluble, bactericidal, concentration-dependent	Extended Gram-negative, some Gram-positive, including *Staphylococcus* spp. (not recommended as sole therapy)	Short half-life (relevant for safety only); nephrotoxicity limiting factor; see text for actions that minimize toxicity
• Fluorinated quinolones • 2nd to 3rd tier • Topoisomerase inhibitor	Enrofloxacin Ciprofloxacin (human) Marbofloxacin Orbifloxacin Levofloxacin (human) Pradofloxacin (3rd-generation veterinary)	Weak base, lipid-soluble, accumulates in phagocytes; bactericidal, concentration-dependent	Extended Gram-negative, including *Pseudomonas*, some Gram-positive, including *Staphylococcus*	Develops high-level, multidrug resistance Ciprofloxacin not orally bioavailable in cats and fair bioavailability in dogs Resistance may be harder to develop toward pradofloxacin. Note unique toxicities
• Sulphonamides, 'potentiated' with diaminopyrimidine • 1st or 2nd tier • Folic acid synthesis inhibitor	Sulfadiazine Sulfadimethoxine Sulfamethoxazole with trimethoprim Ormetoprim	Generally lipid-soluble, bactericidal, (when combined), time-dependent	Gram-negative and Gram-positive, anaerobes; use has been limited by resistance; culture based use recommended, otherwise consider reserving use in critical environment to higher order bacteria (*Actinomyces*, *Nocardia*)	Dogs at greater risk for immune-mediated reactions (low incidence)
• Tetracyclines • 1st tier for intracellular organisms • Ribosomal inhibitor, single subunit	Doxycycline Minocycline	Generally lipid-soluble, bacteriostatic, time-dependent	Gram-negative and Gram-positive aerobes, anaerobes; use has been limited by resistance; culture based use recommended, otherwise consider reserving use in critical environment to intracellular parasites	Minimal distribution to urinary tract
• Macrolides • 2nd to 3rd tier • Ribosomal inhibitor, single subunit	Azithromycin Clarithromycin	Generally lipid-soluble, accumulate in phagocytes; bacteriostatic, time-dependent	Gram-positive, limited Gram-negative aerobes (*Actinomyces*, *Nocardia*); culture based use recommended	Minimal distribution to urinary tract; risk of drug interactions (efflux and drug metabolizing proteins)
• Glycopeptides • 4th tier • Cell wall inhibitor	Vancomycin	Generally water-soluble, bactericidal, time-dependent	*Staphylococcus* (generally including meticillin-resistant); *Enterococcus* spp.; anaerobes (*Clostridium* spp.)	Parenteral route only; oral route for local gastrointestinal treatment
• Rifamycins • 2nd to 3rd tier • RNA polymerase inhibitor	Rifampin	Generally lipid-soluble; accumulates in phagocytes; bactericidal, displays aspects of time and concentration dependency	Gram-positive, generally including meticillin-resistant *Staphylococcus*; anaerobes	Resistance may develop sufficiently rapidly that combination therapy only recommended; discoloured body secretions; potential for hepatotoxicity
• Imidazole • 1st to 2nd tier • DNA inhibitor	Metronidazole	Generally lipid-soluble; bactericidal; concentration-dependent	Obligate anaerobes; protozoa	Central nervous system toxicity (dogs in particular) with rapid administration or high doses

23.4 (continued) Summary of antimicrobials used in critical care, based on chemistry–structure activity relationship (class).

Choosing a drug in the critical patient

Both safety and efficacy must be considered in the selection of an antimicrobial drug in the critical patient. Convenience and cost should be reserved as much as possible for de-escalation decisions. Because animals are eukaryotic and bacteria are prokaryotic, targets of antibacterial drugs tend to be specific to the microbe rather than the host. As such, most antimicrobial drugs are quite safe. Adverse reactions can occur though, especially with some classes of antimicrobials, although frequently these have little to do with the mechanism of antimicrobial action. For example, aminoglycosides are among the most toxic drugs used in critical patients and can lead to reduced glomerular filtration rate and direct renal tubular damage. Their nephrotoxicity might be minimized by assuring the hydration status of the patient, using the drug once daily at doses designed to achieve the targeted pharmacokinetic-pharmacodynamic index (see below), avoiding other nephroactive drugs (such as non-steroidal anti-inflammatory drugs, angiotension-converting enzyme inhibitors or diuretics) and, in the dog, dosing in the morning when glomerular filtration rates are higher.

Empirical therapy

Treatment of life-threatening infections presents a unique challenge to the clinician. Withholding antibacterials in this setting is not an appropriate clinical option, as the infection and resulting inflammation will be likely to overwhelm the patient, resulting in an increase in mortality. Indeed, data in humans have closely linked delay in implementation of an effective antimicrobial to increased mortality (Kumar *et al*., 2006).

Choice of the appropriate antimicrobial is facilitated by an awareness of the most likely infecting pathogens – including nosocomial organisms – and their patterns of antimicrobial susceptibility. Such information ideally reflects a local antibiogram that summarizes the percentage of isolates susceptible to potential therapeutic agents. For example, close to 50% of *Escherichia coli* canine uropathogens in the USA are resistant to ampicillin and 40% to co-amoxiclav (the model drug for ampicillin/sulbactam), indicating that these drugs might not be prudent choices for critical patients. An exception might cautiously be made if it is known that the patient (including any household member) has not been exposed to any antimicrobial therapy in the most recent weeks.

In general, higher-tier antimicrobials (eg, carbapenems, aminoglycosides) should initially be chosen in the critical patient with therapy de-escalating to lower-tier drugs as soon as possible. Note that should antimicrobial therapy be initiated and susceptibility data subsequently indicate that bacteria isolated are not susceptible to the chosen drug, the clinician might continue treatment with the drug, if the patient has responded, until completion of the therapeutic course. If the patient has not responded, addition or substitution of an appropriate antimicrobial is indicated. However, the presence of the antimicrobial may have changed the microflora, and relevance of the originally collected culture to the current situation is not clear.

Bacterial culture and susceptibility

Culture is an essential process for confirming the presence of a bacteria at a presumed site of infection. However, it is of equal importance in guiding antibacterial therapy. Data provided on a culture and susceptibility report are only as good as the collection and handling process of the sample. Samples must be collected in a manner that minimizes contamination. Whenever possible, tissue samples rather than swabs are encouraged. Not only do swabs preclude a colony count – which is important when attempting to discern pathogens from commensals – but swabs can inhibit growth of some organisms. Samples can be submitted either in a bacteriology transport media or in a sterile plain transport tube in accordance with the reference laboratory's guidelines. It is critically important that samples be properly refrigerated. For example, with a doubling time of as little as 20 minutes, *E. coli* in a sample can easily overgrow true infecting pathogens. Sample submission should be accompanied by a detailed history, including prior and current antimicrobial therapy, in order to support correct interpretation of the data. A clinical microbiologist can be a powerful member of the therapeutic decision-making team when considering the relevance of cultured growth to cause of infection. Likewise, a clinical pharmacologist can be an important member of the team when determining not only the most appropriate antimicrobial but also the design of the dosing regimen.

Rather than relying on microbiological reporting that simply classifies organisms as resistant ('R') or sensitive ('S'), use of minimum inhibitory concentration (MIC) is recommended. MIC is the lowest concentration of an antimicrobial that will inhibit the visible growth of a microorganism after overnight incubation. One of the most important methods to discern the drug to which an isolate might be most susceptible is to compare the MIC of the infecting isolate to the plasma or tissue drug concentration that will be achieved at the chosen dose. Alternatively, the target pharmacokinetic-pharmacodynamic index (C_{max}:MIC or T>MIC) might be compared among the drugs (see below).

Ideally, the list of possible drugs for a given patient should comprise those drugs for which the MIC of the infecting organism is furthest below the anticipated peak plasma drug concentration that will be achieved at the chosen dose.

Other factors

Once a list of drugs to which infecting organisms are considered susceptible has been identified, a number of other factors should be considered when selecting the drug, including mechanism of action, ability to penetrate different tissues and potential adverse effects (see Figure 23.4). Mechanism of action is important for several reasons: it determines whether or not the drug acts in a bactericidal fashion; it should be the basis of choosing drug combinations; and it may influence the risk of adverse drug events.

The list of drugs under consideration for a given patient should first be separated into bactericidal and bacteriostatic drugs. Whenever possible, bactericidal drugs should be chosen in the critical patient because such patients are less likely to have immunocompetence to overcome any residual bacterial inoculum left behind. However, caution is recommended: a bactericidal drug will act in a bacteriostatic fashion if sufficient concentrations are not achieved at the site to kill the entire infecting inoculum.

If drugs are to be used in combination, a beta-lactam should be chosen whenever possible because its mechanism of action facilitates movement of other antimicrobials into the cell. However, in some species, including rabbits, beta-lactams also increase the risk of overwhelming endotoxin release, particularly in patients with a very large Gram-negative inoculum.

Among the more important considerations in antimicrobial selection is the site of infection. Lipid-soluble drugs (generally characterized by a volume of distribution that exceeds 0.6 l/kg) should be chosen if there is any concern regarding drug penetrability. This is particularly important for infections located in tissues that are difficult to penetrate (e.g. brain, eye, prostate, testes), or in the presence of marked inflammatory debris. Indeed, for the latter situation, selection of an antimicrobial that accumulates in phagocytes (such as a fluorinated quinolone, clindamycin or the macrolides) should be considered. Drugs that are not eliminated in the urine should not be used for urinary tract infections (e.g. macrolides, doxycycline or minocycline, clindamycin). The presence of biofilm, the importance of which is probably markedly underestimated, may also require lipid-soluble drugs. Most antibacterial drug classes are considered lipid-soluble, with the beta-lactams and aminoglycosides being water soluble.

Although safety is occasionally a factor that influences antimicrobial selection, most classes of antibacterial antimicrobials are considered safe because they target prokaryotic structures rather than the eukaryotic structures of the host. This is less true for antifungal antimicrobials

because fungal organisms are also eukaryotic. Of the classes of antimicrobial drugs that carry a higher risk of adverse effects, the mechanism of toxicity (e.g. aminoglycosides) is not related to the mechanism of antimicrobial action.

Dosing regime

Once an antimicrobial has been chosen, the design of the dosing regimen is the next important step. The first consideration is the choice of route. Initial intravenous administration is the route of choice in patients with life-threatening infections as this generates the most rapid peak concentration of the drug. Alternative routes, including intramuscular and subcutaneous, are not recommended in emergency and critical care settings as the systemic absorption from these sites is unreliable and often delayed due to changes in vascular volume and hydration status.

Design of the dose and interval depends, in part, upon whether or not the drug expresses time or concentration dependency as far as antimicrobial efficacy is concerned. For concentration-dependent drugs (fluorinated quinolones, aminoglycosides), dosing regimens should be designed such that the peak plasma drug concentration (C_{max}) achieved at the site of infection exceeds the MIC of the infecting microbe by at least 10 times. For patients considered to be at increased risk for the presence of resistant organisms, this number might even be higher. In general, doses for fluoroquinolones should always be administered at the highest labelled dose. For both aminoglycosides and fluoroquinolones, once daily administration is appropriate, although for isolates with a higher MIC, twice daily dosing might be appropriate for the fluoroquinolones.

For time-dependent drugs, the design of the dosing regimen is more complicated. Drug concentrations at the site of infection should exceed the MIC throughout a significant portion of the dosing interval. The recommended percentage depends upon the drug: for carbapenems, it might be as short as 25% of the dosing interval, but for aminopenicillins, concentrations ideally will be above the MIC throughout the dosing interval. Because these drugs are characterized by a half-life of approximately 1 hour (see Figure 23.4), frequent dosing and potentially even administration as a constant rate infusion might be the more prudent and less expensive approach. Doses may need to be adjusted further upwards to compensate for the site of infection or the presence of marked inflammatory debris.

The duration of treatment varies depending on chronicity of disease and the location of the infection. Traditional guidelines advocate a 7–10 day course of therapy for simple acute infections and longer courses (3–6 weeks) for more chronic infections or infections located in anatomical areas with poor tissue penetration of the drug; examples include pyelonephritis, pyothorax and bacterial meningitis. In more recent years, however, the medical community has begun to question this dogma due to the lack of supporting evidence and concerns about over-use of antibacterials. Critics of the guidelines increasingly advocate a 3–5 day duration of antibacterial therapy for most infections, including community-acquired pneumonia. The ideal duration of therapy for acute bacterial infections in veterinary patients has not been confirmed using scientific evidence, but therapy beyond 10 days is not likely to be warranted in simple acute bacterial infections such as septic peritonitis. Indeed, the International Society of Companion Animal Infectious Disease has promulgated guidelines for the treatment of several infections, including urinary tract infections. The guidelines acknowledge the lack of evidence supporting therapy that exceeds 5–7 days. Among the advantages of shorter duration of therapy is a decreased risk of adverse reactions. This includes the sulphonamides, for which allergic responses will be minimized if the drug can be administered for a duration of 5 days or fewer.

In the face of therapeutic failure or antimicrobial resistance, antimicrobials might be used in combination. Drugs should be selected rationally, based on mechanism of action and target organisms. Mechanisms of action should complement, rather than antagonize, one another. In general, 'bacteriostatic' drugs that inhibit ribosomes and thus microbial growth (e.g. chloramphenicol, tetracyclines, macrolides) should be avoided in the critically ill patient, particularly in the face of multidrug resistance. Drugs that have a different mechanism of action may act in an additive or synergistic fashion. The prototypical example of synergism is the combination of beta-lactams and aminoglycosides; aminoglycoside penetration into bacteria is facilitated by penicillin-induced cell wall failure. Combination antimicrobial therapy may also be indicated because of the need to treat a polymicrobial infection. Aminoglycosides or fluoroquinolones are often combined with drugs that target anaerobes, such as the beta-lactams, metronidazole or clindamycin. The combined use of selected antibacterials may result in effective therapy against a given microbe, even when either drug alone would be ineffective.

Prevention and treatment of hospital-acquired infections

A hospital- or healthcare-acquired infection (HAI), sometimes referred to as nosocomial infection, is an infection the patient acquires while obtaining treatment for other conditions. These infections have a direct detrimental effect on the patient with increased cost of care and the potential to result in fatal disease. They can also negatively affect the hospital's reputation and may have serious consequences for the profession's future ability to freely prescribe antibacterials.

General advice to care providers

In the clinical environment there is a collective responsibility for the prevention of HAIs, regardless of qualifications. All personnel involved in providing patient care should be educated about standard principles of infection prevention and control, and be familiar with any practice-specific guidelines. They should receive on-site training in hand decontamination and the use of personal protective equipment (PPE), with appropriate supplies available when the staff are delivering patient care. It is equally important to educate pet owners about the benefits of effective hand decontamination, the correct techniques for hand decontamination, and when it is appropriate to use liquid soap and water or alcohol-based hand rubs. These factors are important during hospital visits and also for certain patients in the home environment.

Principles of hand decontamination

Prior to the era of antibacterial therapy, the pioneers of infection control, Ignaz Semmelweis (1818–1865) and

Joseph Lister (1827–1912), identified physician handwashing prior to performing obstetrical and wound examination, respectively, as being key to reducing patient mortality. In the modern era, hand-mediated transmission has been shown to be a major contributing element in the development of HAIs. These infections include both meticillin-sensitive and meticillin-resistant *Staphylococcus aureus* (MRSA), meticillin-resistant *Staphylococcus pseudintermedius*, Gram-negative aerobes and enterococci. This transmission can occur from one patient to another via the hands, or from hands that have become contaminated from the environment. There is a direct clinical threat when these microorganisms are introduced to vulnerable sites such as surgical wounds, intravascular access sites, catheter drainage systems and enteral feeding systems.

When to decontaminate hands

Hands must be decontaminated in the following clinical situations:

- Immediately prior to all episodes of direct patient contact, including aseptic procedures
- Immediately after all episodes of direct patient contact
- Immediately after exposure to body fluids
- Immediately after any contact with a patient's surroundings that could result in hands becoming contaminated, e.g. after taking a dog for a walk from its kennel
- Immediately after removal of gloves.

Which hand decontamination preparation to use

Alcohol-based hand rubs have grown in popularity over the last decade due to a greater awareness of HAIs and also due to major convenience factors associated with these rubs – i.e. there is no need for running water or hand drying equipment. There is also clinical evidence that the alcohol-based hand rubs are more effective at reducing bacterial colonization of a person's hands than aseptic hand washing. They also have direct cost savings over aseptic hand washing, with alcohol-based hand rubs costing up to 50% less. However it is important to recognize that some organisms are alcohol resistant (e.g. *Clostridium difficile*).

Current recommendations are:

- Decontaminate hands with an alcohol-based hand rub except in the following circumstances:
  - When hands are visibly soiled
  - When hands are potentially contaminated with body fluids
  - In clinical situations where there is the potential spread of alcohol-resistant organisms.

To assist with making hand decontamination effective throughout the day and to further reduce the risk of spreading microorganisms via hands it is recommended that:

- Workers are 'bare below the elbows' when delivering direct patient care
- Wrist and hand jewellery is removed
- Fingernails are short, clean and free from nail polish
- Cuts and abrasions are covered with a waterproof dressing
- A new pair of disposable, non-sterile gloves can be worn for all patient contact.

Technique for hand decontamination

An effective hand washing technique requires three stages.

1. Preparation: wet hands under lukewarm, running water before applying liquid or antimicrobial soap.
2. Washing and rinsing: the hand washing solution must come into contact with all surfaces of the hand. Hands should be vigorously rubbed together for a minimum of 15 seconds; attention should be paid to finger-tips, thumbs and areas between the fingers. Hands should be rinsed thoroughly.
3. Drying: drying should be performed with good-quality paper towels. The towels should be disposed of in foot-operated pedal bins.

When using alcohol hand rubs, hands should be free from gross contamination. The hand rub solution must contact all surfaces of the hand. Hands should be vigorously rubbed together with attention paid to fingertips, thumbs and areas between the fingers, until the solution has evaporated.

Use of personal protective equipment

PPE includes the use of gloves, gowns/aprons, facemasks, eye protection or other facial protection. The principal use of PPE is to protect both the staff and patients, and reduce the possibility of transmission of microorganisms within the hospital. The decision to use PPE should be based on an assessment of the level of risk associated with a specific patient care activity/intervention and the risk of contamination of the care provider's clothing and skin with blood, body fluids, secretions and excretions.

Use of gloves

Gloves should be used to prevent hand contamination with organic material and microorganisms and to reduce the risk of transmission to both patients and staff. However, excessive and indiscriminate use may cause adverse reactions and skin sensitivity. To determine whether gloves are required, the caregiver should consider:

- Who is at risk and whether sterile or non-sterile gloves are required
- The potential for exposure to blood, body fluids, secretions or excretions
- Contact with broken skin or mucous membranes.

For the use of gloves to be effective, they should be discarded after each care activity in accordance with national legislation or local policies; washing gloves rather than changing them is seen as unsafe and therefore is not recommended. Within the UK, gloves used for PPE must conform to current EU legislation (marked as medical gloves for single use) and should be appropriate for the task. Non-latex alternatives should be available for workers, owners and other caregivers that have a documented latex sensitivity. It is important, however, that non-sterile polythene gloves should not be used for sterile clinical interventions as they do not provide sufficient protection against microorganisms for healthcare workers or their patients (National Institute of Health and Care Excellence, 2016).

Use of plastic aprons

There is growing use of plastic aprons when interacting with patients as a method of preventing gross contamination

of clothing and to reduce transmission of infectious organisms from patient to patient. All the information surrounding the use of plastic aprons comes from human medicine, where it has been shown that disposable plastic aprons covering nurses' uniforms reduce MRSA contamination and other important HAIs. It is important to be aware that for aprons to be effective at reducing transmission they must be discarded after each patient contact, as the electrostatic nature of plastic aprons causes them to attract bacteria from the surrounding environment; polyethylene plastic aprons can attract up to 83% more bacteria than standard uniforms (Royal College of Physicians, 2012).

It is recommended when delivering patient care that:

- Disposable plastic aprons are worn when there is a risk that clothing could be exposed to blood, body fluids, secretions/excretions
- Long-sleeved, fluid-repellant, disposable gowns are used when there is a risk of excessive splashing of blood, body fluids, secretions and excretions
- Plastic aprons and gowns are used as single-use items for one episode of patient care and they are disposed of correctly.

Placement and maintenance of indwelling devices

Among the factors contributing to the development of HAIs is the clinical need for indwelling devices in critical care patients. The skin is an important part of the adaptive immune system and functions as a physical barrier to pathogens. While the placement of indwelling devices has clinical benefit, breaking this physical barrier provides a convenient pathway for pathogens to access otherwise sterile environments. Only through clinical vigilance can the risk of HAIs via indwelling devices be minimized so that the benefit outweighs any potential risk.

Peripheral intravenous catheters

The use of peripheral intravenous catheters for the administration of fluid therapy and medications is an everyday occurrence in emergency and critical care patients. As intravenous catheters have direct access to the circulation, there is a potential for serious complications if a catheter-related HAI occurs. Standardized techniques for placement and maintenance of intravenous catheters reduce the occurrence of catheter-related HAIs. An example of a standard technique for the placement of an intravenous catheter can be found in Chapter 2.

Peripheral intravenous catheters, if placed correctly and vigilantly maintained, can remain functional for 3–7 days. Having a policy of removing peripheral catheters after a specified number of days does not reduce the incidence or risk of catheter-related infections (Webster *et al*., 2015). Daily visual and manual inspection of the catheter site is mandatory. Signs of catheter complications include redness, swelling, discharge, discomfort/pain and thrombosis. The presence of any of these signs should result in catheter removal and replacement.

Central venous catheters are potentially more susceptible to becoming infected because they are often *in situ* for longer than peripheral intravenous catheters. Central catheters should be inserted in a sterile manner and handled in a similar fashion, i.e. sterile gloves should be worn when handling the catheter or connections, access ports should be cleaned with 70% isopropyl alcohol prior to injections and prior to disconnecting and reconnecting fluid extension lines. Special consideration for sterility should be applied when these catheters are used for providing parenteral nutrition. The presence of glucose and other nutrients in parenteral nutrition provides an ideal medium for bacterial growth so strict adherence to sterile technique at all times is a must.

Urinary catheters

Urinary catheters are used for both patient monitoring and management. Like other indwelling devices, they represent a potential pathway for HAIs and evidence suggests the incidence of bacterial infections may be in excess of 50% (Bubenik *et al*., 2007). Prior to placing an indwelling urinary catheter, it is important to make a clinical judgement whether the benefits outweigh any risks. Examples of patients that may benefit from the placement of an indwelling urinary catheter include those that need urine output monitoring and those with the inability to void urine. Whenever possible the clinician should avoid repeated intermittent passage of a urinary catheter as this will increase the risk of a urinary tract HAI.

The majority of catheter-related urinary tract infections (UTIs) are thought to occur during catheter placement, therefore this procedure should be performed aseptically. Hair around the prepuce or vulva, should be clipped and cleaned using chlorhexidine scrub. To reduce flora within the prepuce and vulva, a dilute chlorhexidine solution can be used to lavage these areas. Sterile gloves should be used to maintain asepsis during handling and placement of the catheter. Once placed, it is essential that a closed collection system is used to minimize the risk of an ascending infection developing, as the absence of a closed collection system has been shown to increase the risk of a catheter-related UTI (Sullivan *et al*., 2010). It is inappropriate to administer systemic prophylactic antibacterials as a method to reduce the occurrence of a catheter-related UTI. Instead, the urine sediment should be carefully monitored daily, and cultures performed if appropriate.

The longer a urinary catheter is in place, the higher the risk of development of a catheter-related UTI. As a result, once they are in place catheter systems need to be maintained properly. General precautions of hand decontamination before and after patient contact plus wearing gloves will aid in the care of these patients. Catheters should be kept free from gross contamination by routine cleaning of the exposed catheter and external genitalia with dilute chlorhexidine scrub. The closed collection system should be prevented from contacting the floor or other potentially contaminated surfaces. When handling the collection system gloves should be worn, and urine should be emptied as clinically indicated, typically every 4–8 hours, in a manner that maintains the closed system.

Chest drains

Chest drains are placed to allow removal of air and/or fluid from the pleural space. Placement should be seen as a surgical procedure and strict aseptic technique should be maintained during placement, including the use of sterile gloves, surgical facemask and hat, a wide surgical field to prevent contamination with hair, and surgical skin preparation. When maintaining a chest drain, strict asepsis should be continued, and a light adhesive dressing should be placed over the insertion site to minimize gross contamination. These should be changed daily or more frequently if required and the insertion site should be inspected for

redness, swelling or discharge. Whenever there is patient contact, hand decontamination is required before and after. Sterile gloves should be worn when handling the chest drain and/or insertion site. It is inappropriate to administer systemic prophylactic antibacterials as a method to reduce the occurrence of HAIs associated with chest drains.

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Useful website

www.iscaid.org/

Chapter 24

Imaging techniques for the critical patient

Andrew Parry and Frances Barr

Imaging techniques should be used with care in critically ill patients, as manipulation and restraint of the patient may be a source of added stress, and existing injuries may inadvertently be exacerbated. It is therefore important to keep the number of procedures to a minimum by selecting the appropriate techniques for a given situation, and to carry out each examination carefully to minimize the need for repeat examinations. At all times, the patient should be handled gently, paying due regard to the existing clinical problem.

Survey radiography

Survey radiography is an invaluable imaging technique, which may be used to define the problem(s) in an individual patient and to monitor progress over a period of time. Detailed descriptions of radiographic positioning for different parts of the body are available elsewhere, but it may be useful to bear the following points in mind:

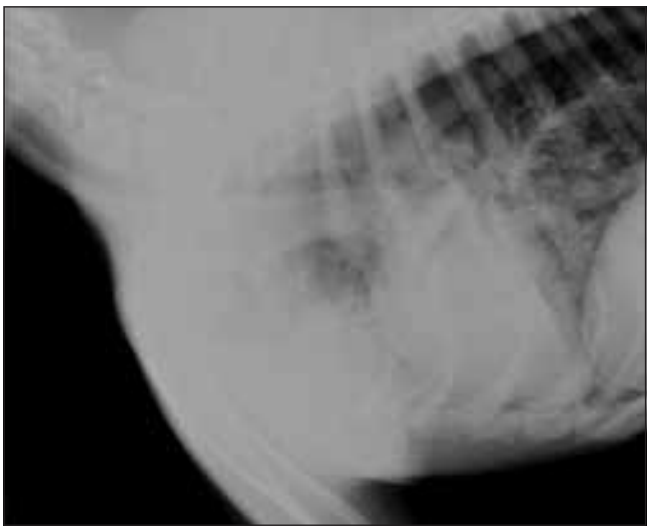
- If general anaesthesia is deemed inappropriate, then adequate positioning and restraint can usually be achieved using foam or plastic troughs, foam wedges and floppy sandbags. Manual restraint is only allowed under 'exceptional clinical circumstances' (Ionising Radiations Regulations, 1999) and is in fact rarely required
- In some clinical situations, it may be preferable to use a horizontal X-ray beam to obtain an orthogonal view rather than repositioning the patient (e.g. in extreme dyspnoea, when lateral recumbency may not be tolerated; or in suspected spinal fracture/dislocation, when it is important to minimize patient manipulation). If a horizontal X-ray beam is used, due regard must be paid to radiation safety
- Ideally, keep exposure time to a minimum. This reduces the risk of movement blur impairing the sharpness of the image
- Examine the resulting images in a careful and systematic fashion, under appropriate viewing conditions, to minimize the risk of missing abnormalities.

Thorax

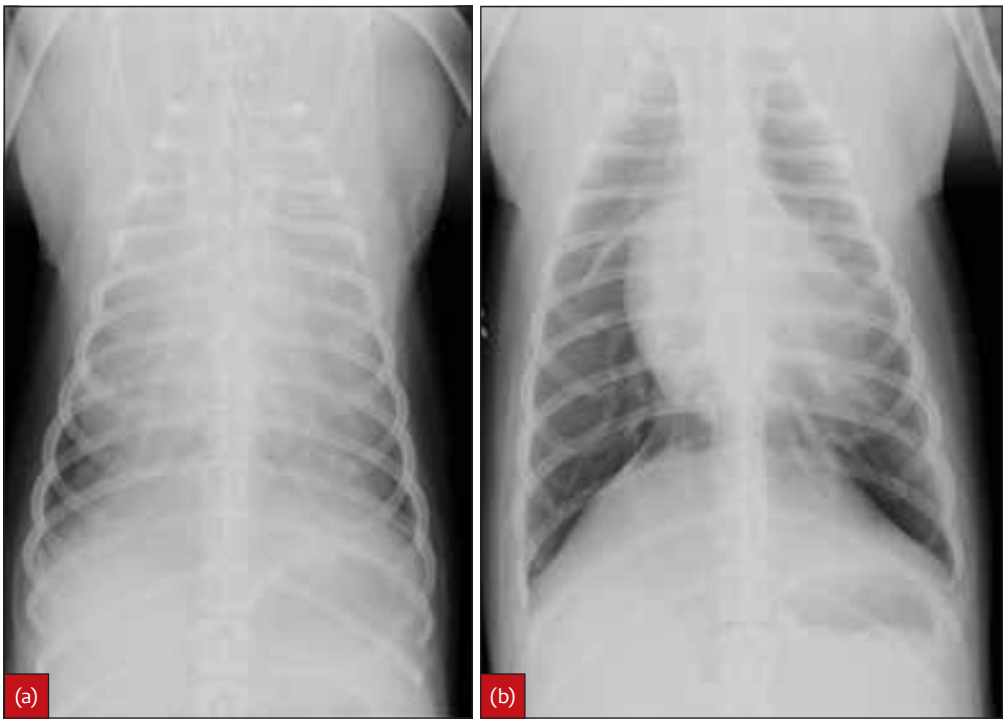
A minimum of two radiographic views is required for complete evaluation of the thoracic cavity: dorsoventral (DV) and lateral. A DV view is generally tolerated well by the patient and is usually preferred to a ventrodorsal (VD) view in critical cases. VD positioning can lead to worsening of respiratory and cardiovascular function in unstable patients. A DV view may be the only view taken before measures are instituted to stabilize the clinical condition of the patient. Substantial information can be obtained from this view alone regarding disease or injury of the thoracic wall, pleural space, heart or lungs.

A recumbent lateral view may not be tolerated by an animal with dyspnoea, in which case an erect lateral view can be achieved using a horizontal X-ray beam with the patient standing or in sternal recumbency (Figure 24.1). In some situations, it may be advisable to take radiographs with the animal in both right and left lateral recumbency. Small masses or areas of consolidation may be seen more clearly in the uppermost (i.e. anti-dependent) lung, where they are surrounded by air-filled alveoli, than in the lower (dependent) lung, which tends to undergo partial collapse.

It is important to include the whole thoracic cavity on each radiograph, and the X-ray beam should be centred and collimated accordingly. The exposure should be made, wherever possible, at peak inspiration, so that the lungs are maximally aerated (Figure 24.2). Occasionally, an exposure may be made deliberately at end expiration to check that the lungs are able to deflate and there is no evidence of air trapping.



24.1 Horizontal X-ray beam standing lateral cranial thoracic radiograph of a skeletally mature dog with severe bronchopneumonia, most likely secondary to aspiration.



24.2 Dorsoventral views of a skeletally mature canine thorax. (a) This radiograph was acquired prior to positive pressure ventilation. Note the increase in soft tissue opacity throughout the lung fields, with border effacement of the cardiac silhouette, with multiple air bronchograms present. (b) This radiograph is from the same patient after a period of positive pressure ventilation. Note the reduction in diffuse soft tissue opacity throughout the lung fields, absence of air bronchograms, and resolution of the border effacement of the cardiac silhouette indicating resolution of the alveolar pattern previously identified.

Computed tomography (CT) can be very useful in patients that present with a thoracic emergency. Provided that they are stable enough to be CT scanned, it may add pertinent information. It is particularly useful in those cases that have sustained extensive trauma (see below).

Abnormalities of the ribs, spine, sternum and soft tissues of the thoracic wall

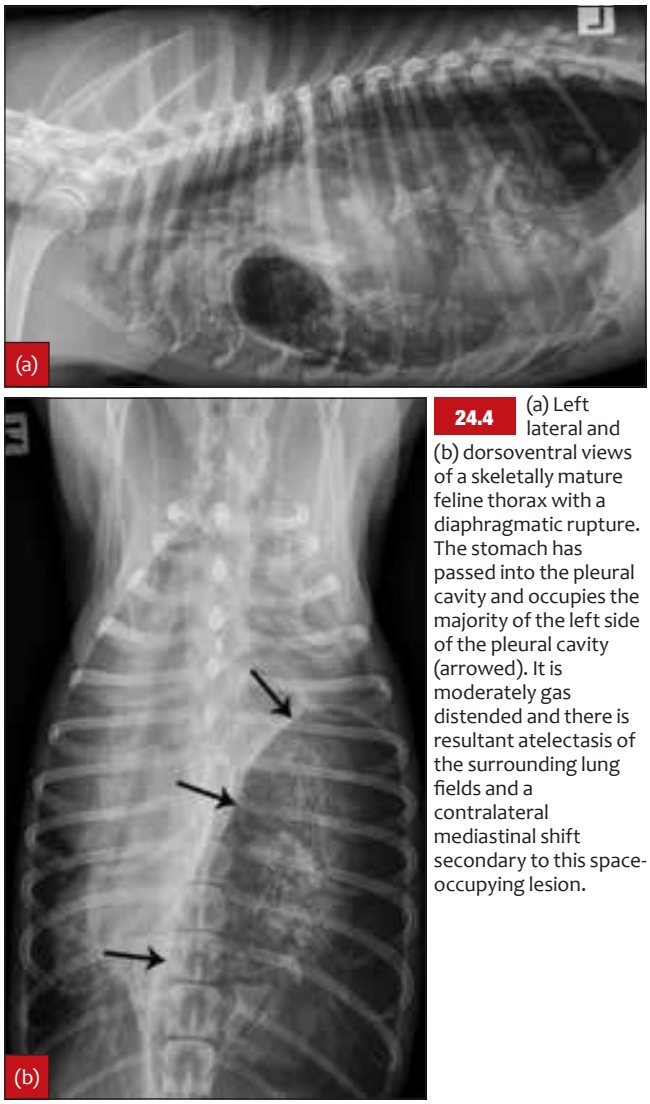
It is important to check the soft tissues of the thoracic wall for swelling, emphysema or radiopaque foreign material. The thoracic spine should be evaluated for evidence of fracture and/or dislocation and, if necessary, further radiographs should be taken centred on the thoracic spine. The sternum should also be assessed. It is important to bear in mind that congenital anomalies of the sternum are not uncommon in dogs and cats (e.g. pectus excavatum) and these must be differentiated from traumatic sternal disruption. Fractures of the ribs are not always easy to identify and a meticulous check should be made along the length of each rib on each radiograph. If several adjacent ribs have multiple fractures, it is wise to check the patient for evidence of 'flail chest' (Figure 24.3).

Abnormalities of the diaphragm

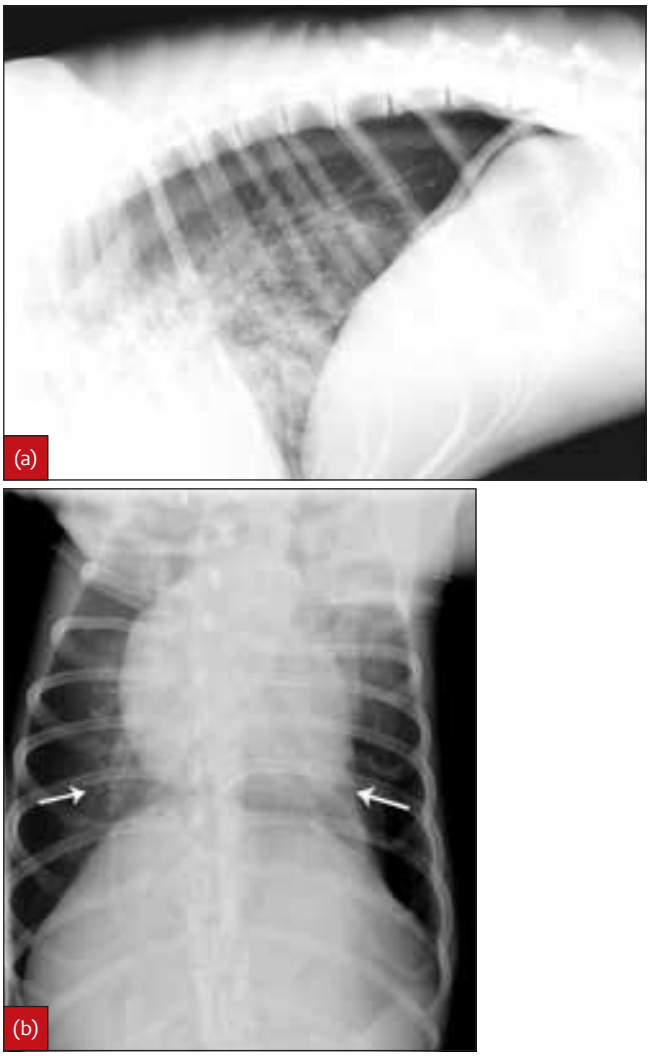
Rupture of the diaphragm is most clearly demonstrated by the passage of abdominal viscera into the thoracic cavity. This results in an overall increase in radiopacity in the thorax, and tubular structures containing gas or food/faecal material may be seen. There is often displacement of intrathoracic structures, together with a corresponding absence of some normal structures from the abdominal cavity. In some instances, the diagnosis is evident on survey radiography (Figure 24.4). In other cases, contrast radiography or ultrasonography may be needed to confirm the diagnosis. Barium can be administered orally and may highlight stomach or intestines within the thoracic cavity. Ultrasonography is particularly useful when a solid parenchymal organ such as the liver or spleen has moved into the thoracic cavity, or when pleural fluid is present. The diaphragm may become partially obscured by pleural fluid or adjacent intrathoracic masses (border effacement).



24.3 Dorsoventral view of a skeletally mature canine thorax after a large dog bite showing evidence of 'flail chest'. Severe trauma has been sustained to the left hemithorax with perforation of the pleural cavity and pulmonary contusion (arrowheads). Segmental rib fractures are present (arrowed), causing a mobile section of thoracic wall. There is severe subcutaneous emphysema, bilateral pneumothorax and severe bilateral pulmonary contusions (alveolar pattern). There is a mediastinal shift to the right.



24.4 (a) Left lateral and (b) dorsoventral views of a skeletally mature feline thorax with a diaphragmatic rupture. The stomach has passed into the pleural cavity and occupies the majority of the left side of the pleural cavity (arrowed). It is moderately gas distended and there is resultant atelectasis of the surrounding lung fields and a contralateral mediastinal shift secondary to this space-occupying lesion.



24.5 (a) Horizontal X-ray beam, standing lateral thoracic radiograph of a skeletally mature dog with progressive severe dyspnoea. There is evidence of pneumothorax and pneumoretroperitoneum. The lung fields are increased in opacity with numerous air bronchograms present. Bronchoalveolar lavage confirmed neutrophilic bronchopneumonia. The pneumothorax is presumed to be secondary to spontaneous rupture of a necrotic area of lung or increased transthoracic forces during laboured respiration. (b) Dorsoventral thoracic view of another dog with bilateral pneumothorax. The lung fields are retracted from the margins of the pleural cavity (arrowed) and increased in opacity secondary to atelectasis.

Abnormalities of the pleural space

Pneumothorax: A small amount of pleural air is most clearly seen on the recumbent or erect lateral radiograph. On the recumbent lateral view, the heart apex appears raised from the sternum and, as the quantity of pleural air increases, the caudal lung lobes start to collapse and retract from the thoracic spine and diaphragm. An erect lateral view is particularly useful in unstable patients that will not tolerate lateral recumbency. On this view, the air accumulates in the dorsocaudal thorax, with retraction of the lung margins at this site. This view may be useful in providing a semi-quantitative evaluation of the amount of pleural air. Collapse (atelectasis) and retraction of the lung lobes are visible on the DV view if moderate or large quantities of pleural air are present (Figure 24.5). If a tension pneumothorax is present, the ribs will be maximally spread and the diaphragm flattened. Intrathoracic structures may be displaced to one side if the problem is unilateral.

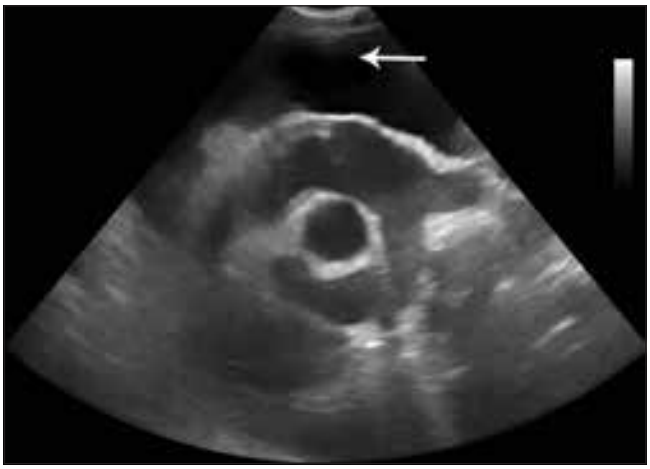
It is important to recognize that collapsed or partially collapsed lung lobes will be of increased radiopacity, even if they are otherwise normal. It is recommended that thoracic radiography is repeated after drainage of pleural air and re-expansion of the lungs, to check for evidence of lung pathology (e.g. bullae, pulmonary haemorrhage).

Pleural fluid: A small amount of pleural fluid in the thoracic cavity is most clearly seen on the DV radiograph as a band of soft tissue separating the margins of the lung lobes from the thoracic wall and running between individual lung lobes (Figure 24.6). On the recumbent lateral view, fluid often lies in the ventral thorax, with partially retracted lung lobes apparently 'floating' on top. As the quantity of fluid increases, it leads to separation of the caudal lung lobes from the thoracic spine and diaphragm. Since non-fat soft tissues and fluid have the same radiopacity, the presence of an intrathoracic mass may be masked by surrounding fluid. Ultrasonography is the imaging modality of choice in such instances as it will allow differentiation between fluid and soft tissue (Figure 24.7).

It is important to note that although imaging confirms the presence of pleural space disease, it may be medically appropriate to perform thoracocentesis prior to imaging if there is a high clinical suspicion of pleural space disease and the animal is unstable (see Chapter 7).



24.6 (a) Lateral and (b) dorsoventral views of a skeletally mature feline thorax. The trachea is elevated on the lateral view, indicating cardiomegaly. There is border effacement of the cardiac silhouette and an increase in soft tissue opacity throughout the thorax. The lung lobes are retracted from the margins of the pleural cavity (arrowed). Pleural fissure lines are visible between the lung lobes (arrowhead). This is indicative of a pleural effusion. The cat was diagnosed with restrictive cardiomyopathy using echocardiography.

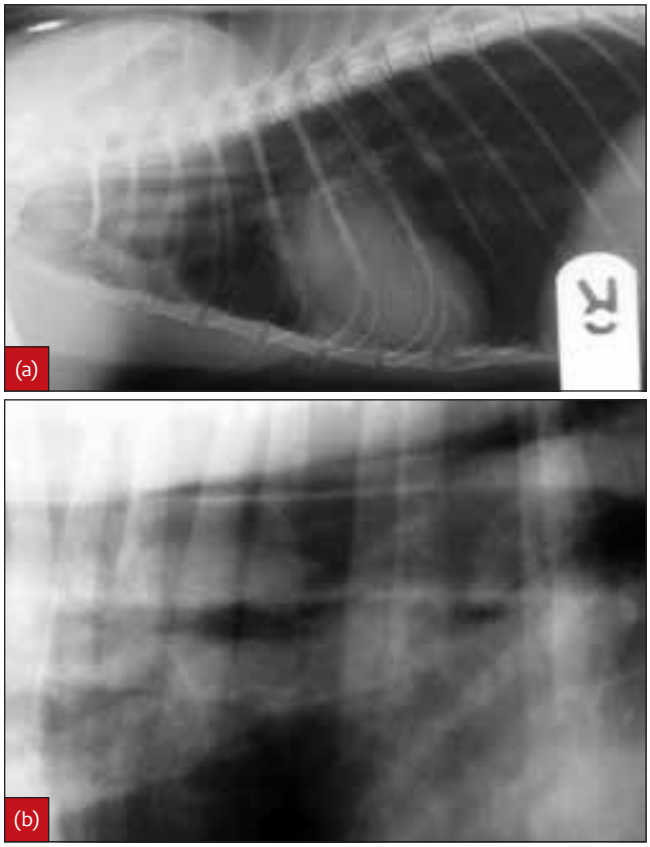


24.7 Right parasternal short-axis view of the cardiac base showing the pulmonary outflow tract and branching of the main pulmonary artery. Anechoic material is identified within the pleural cavity, indicating pleural effusion (arrowed).

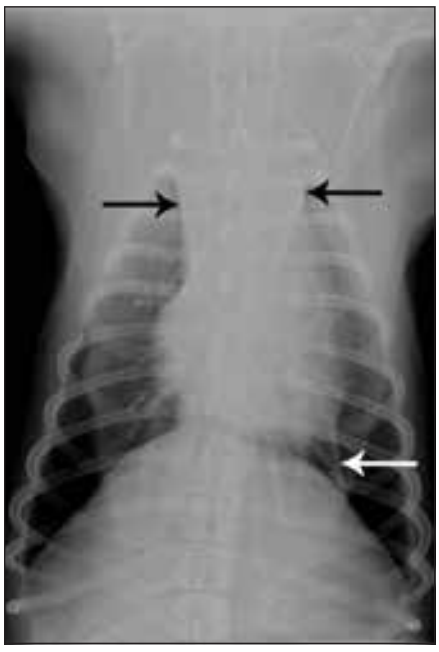
Abnormalities of the mediastinum and structures running within the mediastinum

Air may track within the mediastinum ('pneumomediastinum'), allowing increased visualization of the trachea, oesophagus, heart base and major vessels. This may be a consequence of dyspnoea or blunt thoracic trauma, but may also result from jugular venepuncture or penetrations of the skin of the neck, pharynx, oesophagus or trachea (Figure 24.8).

Fluid within the mediastinum may result in radiographic widening of the mediastinum and 'reverse fissure' formation as fluid insinuates between the lobes of the lung at the hilus (Figure 24.9).



24.8 (a) Right lateral thoracic radiograph of a skeletally mature cat that has sustained trauma, demonstrating a pneumomediastinum. (b) Close-up lateral thoracic radiograph of a dog after being hit by a car. The trachea, oesophagus and great vessels are visible within the cranial mediastinum abnormally well, indicating pneumomediastinum.
(Courtesy of P Mahoney)



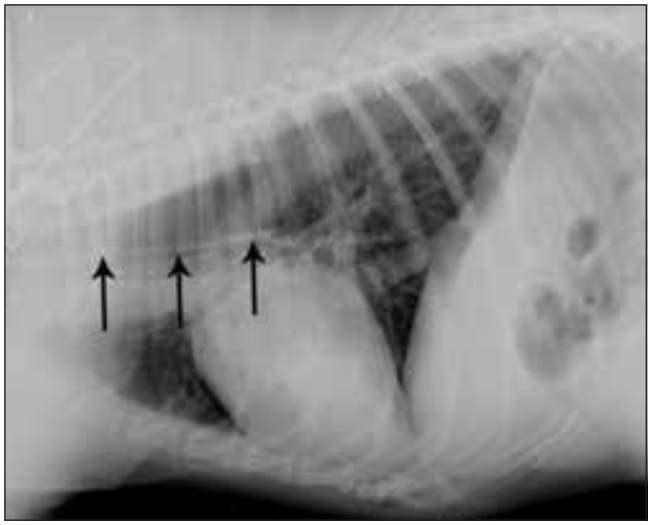
24.9 Dorsoventral view of a skeletally mature canine thorax of a dog that has recently ingested rodenticide. There is marked widening of the cranial mediastinum (black arrows), which measures greater than two vertebral bodies wide. There is widening of the caudoventral mediastinal reflection, indicating the presence of pleural fluid (white arrow). Ultrasonography confirmed the presence of fluid in the mediastinum consistent with mediastinal haemorrhage.

The lumen of the trachea should be carefully checked throughout its cervical and thoracic length. Foreign bodies are generally easily seen, as they are surrounded by air. Localized narrowing of the lumen may be a consequence of a static lesion (e.g. a stricture, granuloma or neoplasm) or a dynamic lesion (e.g. tracheal collapse). Generalized narrowing of the lumen may be a result of tracheal hypoplasia, mucosal oedema or haemorrhage, or severe tracheal collapse (Figure 24.10). Tracheal penetrations result in extensive pneumomediastinum, subcutaneous emphysema and sometimes disruption of the visible tracheal outline. Intrathoracic tracheal rupture is typically associated with the formation of a thin-walled bullous structure within the airway or in place of the normal tracheal walls.

The oesophagus must also be carefully checked throughout its cervical and thoracic length. A little gas within the oesophagus is not unusual, especially in an animal with dyspnoea or under general anaesthesia, but large quantities of gas suggest either gas accumulation proximal to an oesophageal obstruction, or a motility disorder (e.g. megaoesophagus; Figure 24.11). Penetration of the oesophagus usually results in air and/or fluid within the mediastinum. Contrast studies may be required for a full evaluation of the oesophagus.



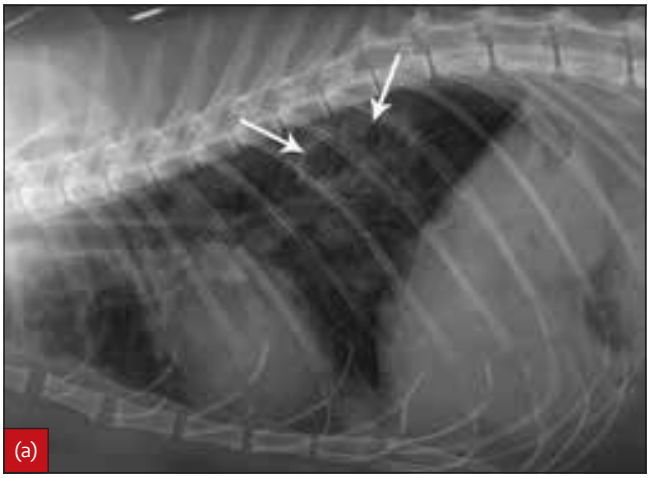
24.10 Lateral view of the thoracic inlet of the same dog as in Figure 24.9. There is marked narrowing of the tracheal lumen in a diffuse fashion, affecting the entire trachea. Ultrasonography confirmed tracheal mucosal thickening, compatible with intramural haemorrhage.



24.11 Right lateral view of the thorax of a skeletally mature dog with a history of regurgitation and a cough. There is marked widening of the intrathoracic oesophagus, which is dilated with gas. The dorsal border of the trachea forms a composite shadow with the ventral border of the oesophagus, called a tracheo-oesophageal stripe sign (arrowed). There is an increase in soft tissue opacity overlying the cardiac silhouette, with occasional air bronchograms. Radiological diagnosis: megaoesophagus with right middle lobar bronchopneumonia from aspiration.

Abnormalities of the lungs

- Well defined soft tissue nodules or masses within the lung generally indicate primary or metastatic neoplasia, although granuloma or abscess formation may also be seen. Gas shadows within a mass can indicate that it is cavitary, with the gas within either an abscess or a necrotic tumour (Figure 24.12). Bullae or cysts usually contain air or air and fluid, and have thin, well defined walls.
- Flooding of the alveoli with blood, inflammatory or oedema fluid, or filling of the alveoli with neoplastic cells, results in areas of increased opacity within the lung. Small ill-defined areas which blur the normal pulmonary vascular pattern may coalesce to form large areas of increased opacity with air-filled bronchi running through them ('air bronchograms'; termed an 'alveolar' lung pattern). The distribution of such changes may help narrow the list of differential diagnoses. For example, cardiogenic oedema in the dog often begins with a perihilar distribution (Figure 24.13), while aspiration pneumonia characteristically affects the ventral portions of the cranial and middle lobes (Figure 24.14).

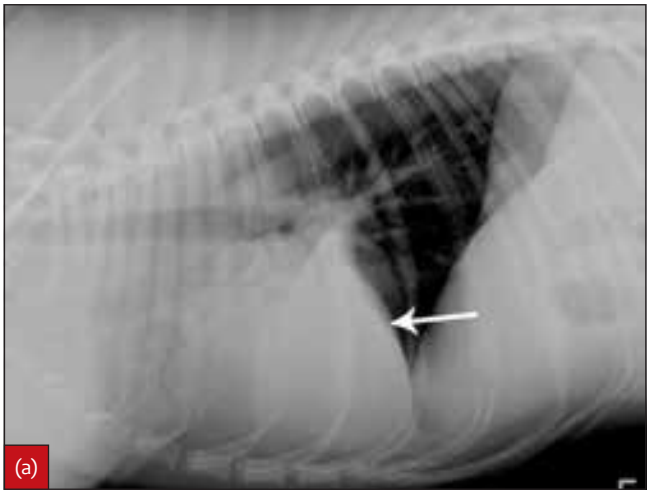




24.12 (a) Right lateral and (b) slightly rotated dorsoventral views of a skeletally mature cat with a chronic cough. There is marked widespread bronchial thickening, with a cavitary mass present in the right caudal lung field (arrowed). Multiple small soft tissue opacity interstitial nodules are also visible. The diagnosis in this case was bronchogenic carcinoma with multiple metastases.



24.13 Left lateral view of the thorax of a skeletally mature dog that presented with severe dyspnoea. The dog was treated with furosemide 4 hours previously. There is a marked increase in soft tissue opacity, with multiple air bronchograms present, most obviously around the hilus of the lung and in the caudodorsal lung fields. The cardiac silhouette is markedly enlarged and left atrial dilatation is visible. There is moderate border effacement of the caudodorsal aspect of the cardiac silhouette, secondary to the overlying lung tissue pathology. Radiological diagnosis: congestive heart failure and cardiogenic pulmonary oedema. On echocardiography, severe dilated cardiomyopathy was seen.





24.14 (a) Left lateral and (b) dorsoventral views of a skeletally mature canine thorax. The dog presented with a short history of severe acute dyspnoea and pyrexia. There is a marked increase in soft tissue opacity in the cranial aspect of the thorax with consequent border effacement of the cranial mediastinum and cardiac silhouette. On the lateral view, there is a lobar sign overlying the cardiac silhouette. This is an interface between the consolidated right middle lobe and the relatively aerated right caudal lobe (arrowed). Radiological diagnosis: bronchopneumonia, most likely secondary to aspiration. (continues) ▶



24.14 (continued) (c) Left lateral thoracic radiograph of the dog after successful management.

- Collapse of a lung lobe may result in a similar radiographic appearance to that of alveolar filling. While lobar collapse (atelectasis) may be a consequence of disease processes, such as air or fluid in the pleural cavity or a space-occupying lesion, it may also be a consequence of prolonged recumbency. If the increase in lung opacity is due to recumbency, it is often associated with radiographic evidence of a loss of lung volume on that side (e.g. raising of the hemidiaphragm on the same side and/or shifting of the heart to that side; ipsilateral mediastinal shift). This is important to remember when dealing with critically ill patients, which may spend much of their time recumbent (Figure 24.15).
- The walls of the major bronchi are usually visible radiographically as thin tapering radiopaque lines and rings. The bronchial markings may become more prominent if the bronchial walls become thickened or calcified, or if there is peribronchial cellular infiltration. Some increase in bronchial markings is to be expected as the animal ages, but may also be associated with airway disease.



24.15 Dorsoventral radiograph of a skeletally mature canine thorax. There is an increase in soft tissue opacity in the left hemithorax, making evaluation of the left lung difficult. There is also an ipsilateral mediastinal shift, with the cardiac silhouette displaced to the left. Radiological diagnosis: atelectasis. This dog had been sedated and placed in left lateral recumbency prior to the radiograph being obtained.

Abnormalities of the heart

The normal shape and size of the cardiac silhouette in the cat and dog are well established. In the dog, there is marked variation with breed and conformation. On a lateral radiograph, for example, a deep-chested dog normally has a narrow upright heart, while a barrel-chested dog normally has a rounded heart with much greater sternal contact. There is far less variation among breeds of cat. Assessment of the shape and size of the cardiac silhouette should be made using lateral and DV radiographs, taking into account breed and conformation. Suboptimal positioning of the patient, and in particular rotation of the thorax, will change the appearance of the cardiac silhouette. Be wary, therefore, of interpreting changes in the shape of the heart if the thorax is rotated.

- If the cardiac silhouette is smaller than normal, this may indicate hypovolaemia (e.g. blood loss, dehydration, Addison's disease).
- If the cardiac silhouette is larger than normal, this may indicate enlargement of one or more chambers of the heart. Whilst by no means accurate, changes in the shape of the heart may help suggest which chambers or great vessels are involved. For example, an increase in the height of the heart on the lateral radiograph, with bulging of the dorsocaudal angle, indicates left chamber enlargement (Figure 24.16). An increase in the craniocaudal diameter of the cardiac silhouette is often seen with right chamber enlargement.



24.16 (a) Right lateral and (b) dorsoventral views of a skeletally mature canine thorax. The patient presented with a chronic progressive history of a soft cough and exercise intolerance. There is marked cardiac enlargement, with an increase in dorsoventral cardiac height on the lateral view, and an increase in width on the dorsoventral view. The left atrium is enlarged, seen as a soft tissue opacity at the dorsocaudal aspect of the cardiac silhouette on the lateral view and as a soft tissue opacity between the caudal lobar principal bronchi on the dorsoventral view. The pulmonary veins are also enlarged.

- A round, globular cardiac silhouette on both radiographic views is often seen in association with pericardial fluid. Ultrasonography is the technique of choice for confirming the diagnosis and for searching for any underlying causes.

Abdomen

A minimum of two radiographic views is necessary for complete evaluation of the abdominal cavity: VD and lateral. A VD view is preferred to a DV view, because the abdomen presents as a thinner structure for the X-ray beam to traverse, and the pelvic limbs are not superimposed on the area of interest. However, there may be situations (e.g. dyspnoea or hypotension) where it is not desirable to turn the animal on to its back, in which case a DV view of the abdomen may be used. In an unstable patient, it is often acceptable to take one radiograph of the abdomen (preferably in lateral recumbency) for an initial evaluation before taking measures to stabilize the clinical condition. If clinically appropriate, food should be withheld for 12 hours prior to radiography and the animal should be given the opportunity to defecate, so that food/faecal material does not obscure other structures in the abdomen.

It is important to include the whole abdominal cavity. In large dogs, it may be necessary to take two separate radiographs centred on the cranial and caudal abdomen, respectively. The exposure(s) should ideally be made at the end of expiration, when abdominal thickness and respiratory movement are minimized. When the abdominal thickness exceeds 10 cm, the use of a grid will improve image quality by reducing the amount of scattered radiation reaching the film. CT, particularly using an iodinated contrast agent, can be very useful for assessing the abdomen, provided the patient is stable enough to be scanned. It is most useful for those cases where conventional radiography and ultrasonography are unsatisfactory (e.g. very large or obese patients, and panting or hyperventilating patients). This is discussed in more detail below.

Abnormalities of the abdominal wall

The soft tissues of the abdominal wall should be checked for integrity, swelling, emphysema or radiopaque foreign bodies. The lumbar spine should be assessed for evidence of trauma, bone proliferation or destruction. If necessary, further radiographs should be taken centred on this area.

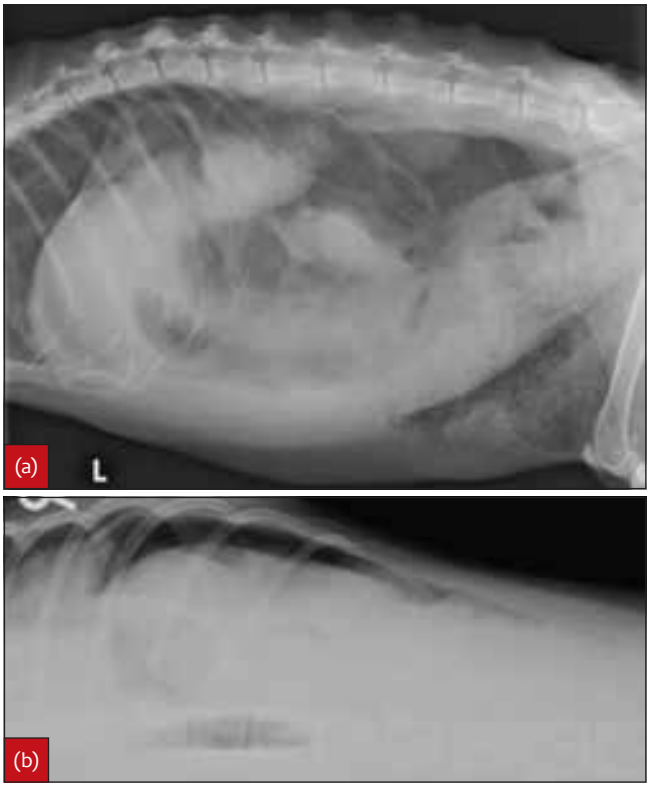
Abnormalities of the abdominal cavity

- Contrast resolution in the abdominal cavity, allowing differentiation of the various soft tissue structures, is normally provided by fat. Consequently, poor abdominal serosal detail may be seen in very young or very thin animals. However, the presence of fluid in the abdominal cavity will also obscure detail (reducing contrast resolution); a small or moderate amount of fluid blurs fine detail, while larger quantities result in a homogeneous opacity throughout the abdomen, relieved only by gas/food/faecal material in the gastrointestinal tract.
- Peritonitis results in blurring of abdominal detail, either throughout the abdomen or in a localized area, due to the production of exudate. There may also be a mottled effect due to the formation of adhesions and pocketing of fluid. Intestinal loops in the area may be dilated and static due to paralytic ileus, corrugated due to irritation, or abnormally bunched due to adhesions.

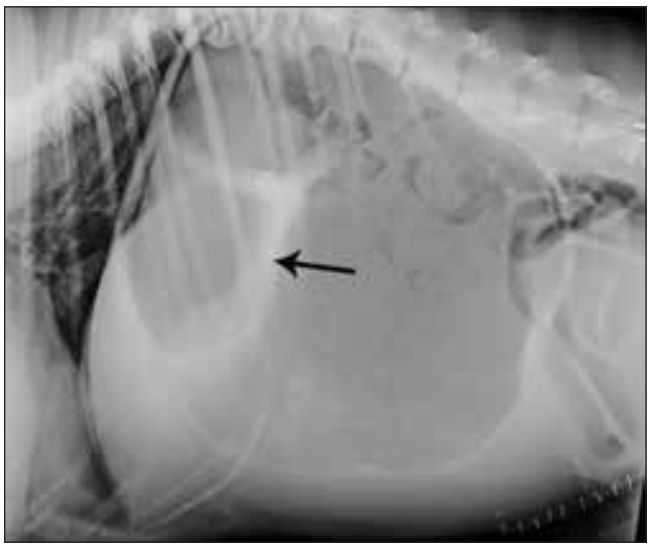
- Air in the abdominal cavity ('pneumoperitoneum') may be seen as irregular accumulations of gas which cannot be localized within the bowel, sometimes accumulating between the liver and the diaphragm. If there is no penetrating wound of the abdominal wall, or recent laparotomy, a pneumoperitoneum is highly suggestive of perforation of the gastrointestinal tract. A decubitus lateral view is often useful to confirm the presence of pneumoperitoneum (Figure 24.17). This is undertaken by positioning the patient in left lateral recumbency and obtaining a radiograph of the cranial portion of the abdomen, using a horizontal beam. Care should be taken that the local rules allow use of a horizontal beam.

Abnormalities of the gastrointestinal tract

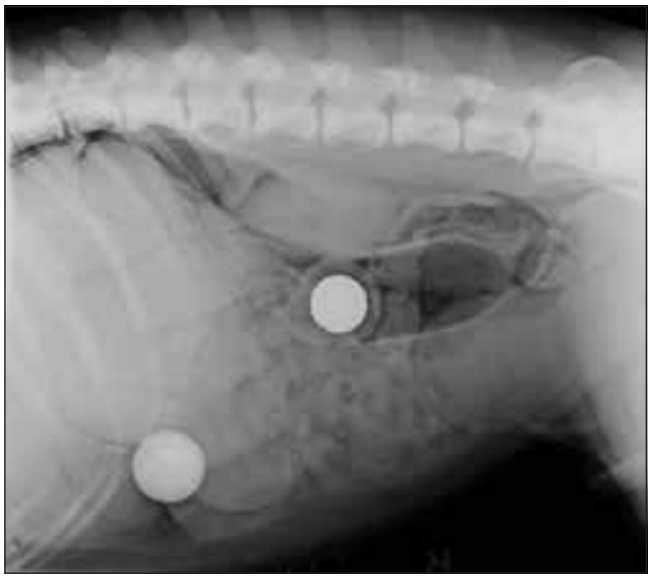
- The stomach is a naturally distensible organ and so varies greatly in size. Excessive distension of the stomach may be an acute phenomenon (as part of the gastric dilatation–volvulus syndrome) or may be more chronic. Acute gastric distension is usually due to food or gas accumulation. When volvulus is present, transposition of the fundus and pylorus may be recognized, especially evident on the right lateral view, and soft tissue bands may be seen compartmentalizing the stomach (Figure 24.18). Chronic distension due to gastric outflow obstruction or motility disorders is usually associated with fluid and sometimes the collection of particulate 'gravel' in the pyloric region.
- The small intestine normally contains a mixture of gas and fluid. The diameter of small intestinal loops does not normally exceed 1.6 x the height of the vertebral body of the 5th lumbar vertebra (L5). Undue fluid or gaseous distension of small intestinal loops may be seen in cases with generalized paralytic ileus (e.g. with infectious gastroenteritis, after a laparotomy, due to hypokalaemia) or secondary to a mechanical obstruction (Figure 24.19). With generalized ileus, bowel loops tend to be uniformly distended, whereas with a mechanical obstruction both dilated and normal loops are usually present. In cases of chronic partial intestinal obstruction, particulate material may accumulate proximal to the obstruction – a so-called 'gravel sign'. The cause of an obstructive process may be apparent on survey radiographs (e.g. radiopaque foreign body), but in other cases contrast studies or ultrasonography may be required.
- The normal large intestines may contain gas or faecal material. If an enema has been given, or if the patient has diarrhoea, the contents may be fluid.
- Displacement of any part of the gastrointestinal tract may be useful evidence of other disease processes. For example, displacement of sections of the gastrointestinal tract into the thoracic cavity or into the subcutaneous tissues indicates loss of integrity of the abdominal boundaries (Figure 24.20). A change in the shape and size of the liver often results in gastric displacement. Any abdominal mass can displace the small intestine. The descending colon may be displaced dorsally by an enlarged prostate gland or ventrally by enlarged sublumbar lymph nodes.



24.17 (a) Right lateral abdominal radiograph of a skeletally mature cat with a history of anorexia and weight loss. The radiograph was obtained after endoscopy. There is marked pneumoperitoneum with increased serosal detail visible throughout the abdomen. In the ventral abdomen, there is border effacement of the abdominal viscera, secondary to the presence of peritoneal fluid. There is also evidence of subcutaneous emphysema within the inguinal region. There are only six lumbar vertebrae present. Ultrasonography confirmed a grossly thickened stomach and small intestine. Histological diagnosis was lymphoplasmacytic gastritis and enteritis with gastric ulceration, presumably leading to perforation. (b) Horizontal X-ray beam decubitus ventrodorsal view of a skeletally mature dog with a history of vomiting and abdominal pain. Peritoneal gas is visible accumulating anti-dependently within the cranial abdomen around the pylorus and liver lobes. Pneumoperitoneum confirmed that this represented an abdominal emergency, and gastric perforation was confirmed on laparotomy. The dog had been treated with long-term non-steroidal anti-inflammatory drugs for degenerative joint disease.



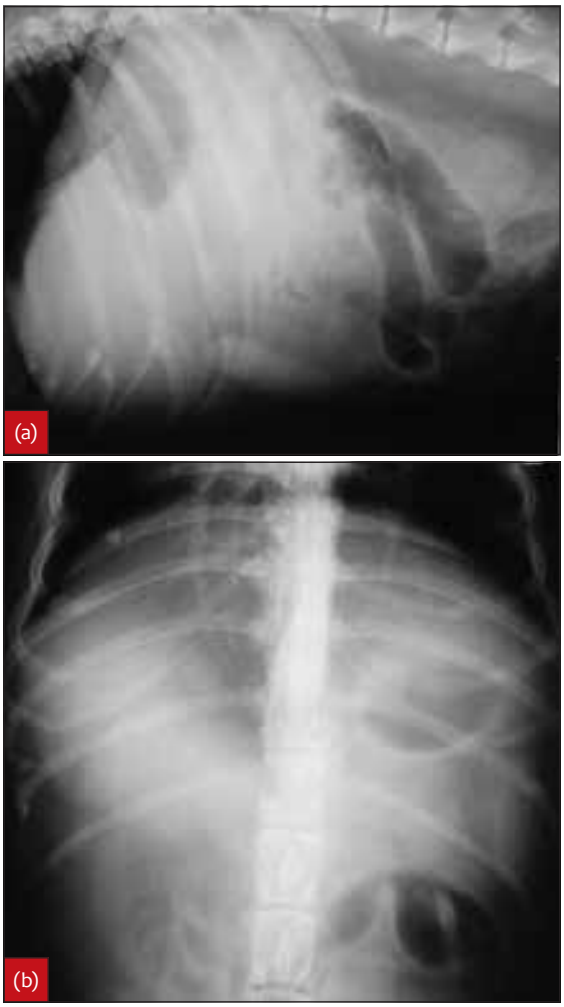
24.18 Left lateral view of the abdomen of a skeletally mature dog that has had a recent coeliotomy. The stomach is grossly dilated with gas. The pylorus lies cranial and dorsal to the fundus and there is a soft tissue band (arrowed) between it and the gastric body (compartmentalization). There is a loss of serosal detail, indicating the presence of peritoneal fluid. Gas is present within the peritoneal cavity, indicating pneumoperitoneum, secondary to the recent abdominal surgery. Radiological diagnosis: gastric dilatation–volvulus (GDV) syndrome. Note that a right lateral radiograph is typically recommended as the most valuable view to document the presence of GDV.



24.19 Right lateral radiograph of a skeletally mature canine abdomen. The dog has undergone recent surgery to remove a gastric foreign body. There is evidence of pneumoperitoneum and peritoneal effusion. Two further radiopaque foreign bodies are present within the small intestine. They are characterized by a central mineral opacity with a peripheral soft tissue opacity. The small intestine is markedly dilated, compatible with complete obstruction (mechanical ileus). Two golf balls were removed at laparotomy.



24.20 Right lateral radiograph of a skeletally mature canine thorax of a dog with a history of weight loss, vomiting and intermittent abdominal bloating. Loops of small intestine are visible within the thorax, overlying the normal thoracic structures (arrowed). There is border effacement of the cardiac silhouette. Radiological diagnosis: diaphragmatic rupture.



24.21 (a) Left lateral and (b) ventrodorsal views of a skeletally mature canine abdomen of a large-breed dog with a history of acute vomiting. There is an increase in soft tissue opacity, accompanied by a loss of serosal detail in the cranial abdomen caudal to the stomach. The transverse colon is displaced caudally. On the ventrodorsal view, there is a poorly defined increase in soft tissue opacity within the cranial right aspect of the abdomen. Ultrasonography confirmed the presence of pancreatitis and minimal peritoneal effusion.
(Courtesy of Elizabeth Baines, Willows Referral Service)

- The normal pancreas is not visible radiographically, but detection of a mass or evidence of localized peritonitis in the right cranioventral abdomen should lead to the suspicion of pancreatic disease (Figure 24.21).

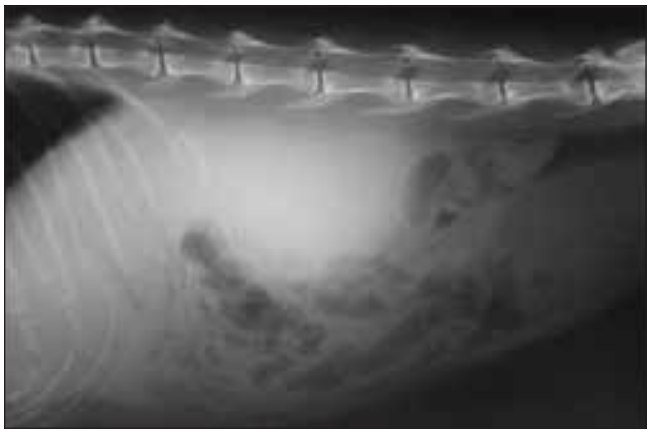
Abnormalities of the liver and spleen

- Symmetrical hepatic enlargement results in extension of the ventral liver lobes well beyond the last rib, and often the tips of these lobes become rounded. The pyloric region of the stomach is pushed caudally and dorsally, resulting in an unusually horizontally positioned stomach. This is called tilting of the gastric axis. The gastric axis is a theoretical line drawn from the gastric fundus to the pylorus. This line should lie somewhere between perpendicular to the spine and parallel with the ribs. With focal asymmetrical enlargement, the normal triangular shape of the liver is lost (Figure 24.22).
- When the liver is unusually small, the ventral lobes lie well within the costal arch and lose their normal triangular shape. The stomach is displaced cranially and becomes unusually upright. The spleen may also move cranially to lie within the costal arch. It should be remembered that the liver has a large functional reserve, and the radiographic detection of a small liver is not necessarily of clinical significance.
- The spleen is a very mobile organ and is extraordinarily variable in both size and position. However, it is usually smooth in outline, with a triangular or elongated shape, and departures from this may be considered abnormal.





24.22 (a) Right lateral and (b) slightly rotated ventrodorsal views of a skeletally mature Persian cat with anorexia and weight loss. There is marked enlargement of the hepatic silhouette with caudal displacement and tilting of the gastric axis. The left kidney is also markedly enlarged (arrowed), with a normal appearance of the right kidney. There is incidental adrenal mineralization. Radiological diagnosis: left renomegaly and hepatomegaly. On ultrasonography, there were multiple cystic cavitary lesions throughout the liver and kidneys.
(Courtesy of P Mahoney)



24.23 Right lateral abdominal radiograph of a skeletally mature cat with anorexia, weight loss and polydipsia. There is marked enlargement of the renal silhouette, which measures approximately 3.5 x the length of the vertebral body of L2 (normal range = 2.4–3.0 x L2). There is ventral displacement of the transverse and descending colon.
(Courtesy of Elizabeth Baines, Willows Referral Service)



24.24 Right lateral abdominal radiograph of a skeletally mature dog. There is marked heterogeneous mineralization of the adrenal glands, which are visible in the dorsal cranial retroperitoneum, dorsal and cranial to the kidneys (arrowed). The dog had no clinical signs that related to adrenal disease. This finding was considered incidental.

Abnormalities of the urogenital tract

- Renal enlargement may be smooth and symmetrical (e.g. hydronephrosis, amyloidosis; Figure 24.23) or irregular (e.g. renal neoplasia, polycystic disease). The accumulation of fluid between the kidney and its capsule may mimic renal enlargement. Reduction in renal size may be associated with renal dysplasia, hypoplasia or chronic parenchymal disease. Renal calculi may be recognized if they are radiopaque. Further information about renal architecture and the ureters requires the use of contrast studies and/or ultrasonography.
- The adrenal glands lie medial to the cranial pole of each kidney. In the dog, the presence of calcification or a mass in this region often indicates adrenal neoplasia (Figure 24.24). In the cat, adrenal calcification may be a normal finding.
- The bladder normally lies in the caudoventral abdomen, and is variable in size. Identification of a bladder does not preclude a small tear in the bladder or urethra, and confirmation or exclusion of these possibilities requires the use of contrast studies. Radiopaque calculi may be identified on survey radiographs, but for further information, proceed to contrast studies and/or ultrasonography.
- The prostate gland lies at the neck of the bladder in the male dog and cat. Enlargement of the prostate gland in the dog results in cranial displacement of the bladder and sometimes dorsal displacement of the rectum/descending colon. While a degree of enlargement is normal in entire dogs as they age, enlargement may also be associated with prostatic disease (Figure 24.25).
- The normal non-gravid uterus is not usually visible radiographically, except in very fat animals. Enlargement of the uterus may result in separation of the bladder from the descending colon by a soft tissue tubular structure and the identification of coiled, distended loops cranial to the bladder. Until fetal skeletal mineralization is detectable in the last trimester of pregnancy, it may be difficult to differentiate uterine enlargement due to pregnancy from that due to disease such as pyometra. Ultrasonography is helpful in this situation.



24.25 Right lateral abdominal radiograph of a dog that had a history of dysuria. There is slight enlargement of the prostate gland, caudal to the bladder (arrowed). The bladder appears moderately enlarged. Prostatic wash was consistent with benign prostatic hyperplasia.

Head

Accurate positioning of the patient is particularly important when undertaking radiography of the head and pharynx. Even slight rotation can result in misdiagnosis, since the anatomy of the area is relatively complex. It is, therefore, preferable to have the patient positioned under general anaesthesia. Occasionally, radiographs may be taken of a conscious patient, but it should be appreciated that positioning is likely to be suboptimal and all but gross lesions may be missed (Figure 24.26). This should therefore be reserved for initial evaluation of a critically injured and unstable patient. Once the patient has been stabilized, a complete radiographic examination under general anaesthesia should be considered. If available, CT may be preferred; it often provides better visualization of lesions than survey radiographs, especially in trauma patients. Several specialized views are described for different regions of the skull, such as the frontal sinuses, temporomandibular joints and tympanic bullae. It is necessary to plan the examination carefully so that all areas under suspicion, based on the clinical examination or standard radiographic views, are fully evaluated. Film within flexible cassettes or specialized views can be useful for intra-oral radiography of the maxilla/nasal chambers, the mandible and individual teeth.



24.26 Right lateral skull radiograph of a skeletally immature dog with pain on opening the mouth. There is marked sclerosis of the mandible and calvarium. A smooth periosteal reaction is present along the ventral aspect of the horizontal mandibular body. Radiological diagnosis: craniomandibular osteopathy.

- Check the soft tissues of the head for swelling, emphysema and radiopaque foreign material.
- Evaluate the bone contours of the skull for disruption (usually traumatic), or bone destruction or proliferation (usually associated with neoplasia or infection).
- Check that the oro- and nasopharynx, the larynx and the cervical trachea are air filled and of a normal calibre.

Magnetic resonance imaging (MRI) or CT may be indicated once the patient has been stabilized, in order to evaluate intracalvarial structures, the nose, and complex fractures (see below).

Spine

As with the head, accurate positioning of the spine is vital if the maximum amount of diagnostic information is to be gleaned from the radiographs. Therefore, general anaesthesia is usually required. If fracture/dislocation of the spine is suspected, survey radiographs may be taken with the animal conscious for a preliminary assessment of the site of the lesion and degree of damage. The patient may be kept in one position (lateral or sternal recumbency) and orthogonal views obtained by use of a horizontal and vertical X-ray beam.

The principles behind accurate positioning of the spine for radiography are:

- To keep the spine parallel to the cassette. This may involve padding areas that naturally sag (typically the neck and the lumbar region)
- To avoid any axial rotation
- To avoid bending of the spine to one side and undue flexion or extension. Specific stressed views in hyperflexion or hyperextension may be used after the standard views have been assessed, depending on the precise problem suspected.

A minimum of two views is required for complete evaluation of the spine: lateral and VD or DV. It is important to include only a small section of the spinal column on each radiograph, with accurate centring and collimation. This is because divergence of the X-ray beam towards the periphery of the X-ray film results in a slightly oblique view of the vertebrae and intervertebral disc spaces, which is not ideal for interpretation. When patient positioning is suboptimal, there is likely to be rotation of the spine. Take care in such cases not to misinterpret asymmetrical positioning of transverse processes or articular facets as evidence of injury.

The radiographs should be checked for:

- The number and alignment of the vertebrae. Remember that a minor malalignment does not necessarily reflect minor spinal cord damage, as the displacement at the time of the injury may have been far greater
- The shape of the vertebrae. Some changes in shape may be due to developmental anomalies (such as block vertebrae, hemivertebrae) while others may be associated with disease processes (e.g. compression fractures)
- Fractures of the vertebrae, including the spinous and transverse processes and the articular facets as well as the vertebral bodies (Figure 24.27)



24.27 Right lateral radiograph of the neck of a skeletally mature dog with neck pain after running into a tree. There is a short oblique fracture of the body of C2. The body of the vertebra is divided and the caudal aspect is dorsally displaced. This caused ventral impingement of the vertebral canal.

- Bone proliferation (e.g. associated with trauma, infection, neoplasia, nutritional disorders) or bone destruction (e.g. infection, neoplasia)
- Evidence of intervertebral disc disease (i.e. narrowing of the intervertebral disc space and/or intervertebral foramen; calcification of disc material with or without displacement).

It may be necessary to proceed to contrast studies after studying the survey radiographs in order to demonstrate the site and severity of any spinal cord compression. MRI or CT may be preferred to contrast studies where these modalities are available (see below).

Contrast radiography

Contrast radiography is indicated in the following situations:

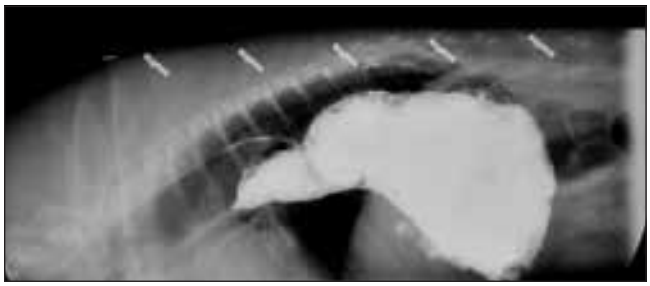
- When survey radiographs do not demonstrate a lesion, but the clinical examination and other diagnostic tests suggest that a lesion is present
- When survey radiographs do show a lesion, but further information is required in order to allow rational treatment to be instituted and an informed prognosis given.

It is important that a good survey radiographic examination precedes the contrast study. This ensures that the appropriate exposure factors are used for the contrast examination, confirms that the contrast technique is indeed necessary and appropriate, and ensures that no lesions are visible on the survey radiographs that may subsequently be masked by contrast medium. Make sure that everything you may require is ready at the beginning of the procedure and that the examination is carried out carefully and thoroughly.

Detailed descriptions of recommended protocols for contrast examinations may be found in standard texts and may differ from the procedures given here, as a result of personal preference. It is very important to note the additional factors listed below.

Oesophageal contrast studies

- General anaesthesia is contraindicated because of the risk of regurgitation and aspiration. Drug-induced decreases in oesophageal motility will also preclude assessment of oesophageal function. In addition, the normal oesophagus may appear dilated during general anaesthesia (Figure 24.28).



24.28 Oblique barium oesophagram of a dog with a history of regurgitation. The study shows sliding of the gastric cardia into the caudal mediastinum and moderate gas dilatation of the oesophagus. Radiological diagnosis: sliding hiatal hernia. The lesion was not identified on survey abdominal radiographs.
(Courtesy of P Mahoney)

- Oesophageal contrast studies are usually contraindicated in very dyspnoeic or collapsed patients because of the risk of aspiration.
- Some authorities argue that a water-soluble iodinated contrast medium should be used in preference to barium if an oesophageal perforation is suspected, as barium is inert and will persist in the thoracic cavity. If water-soluble iodinated contrast media are chosen, it should be remembered that they tend to be very bitter in taste (so may not be accepted as readily as barium) and ionic iodinated agents are also hypertonic (so that inadvertent inhalation may lead to pulmonary oedema).
- Liquid contrast medium is useful for outlining abnormalities of the oesophageal wall (e.g. ulceration, neoplasia, diverticula), intraluminal masses or foreign bodies, or for demonstrating a perforation.
- It may be useful to use contrast medium mixed with food to show a partial oesophageal obstruction or to fill a dilated oesophagus completely.

A procedure for oesophageal contrast studies is shown in Figure 24.29.

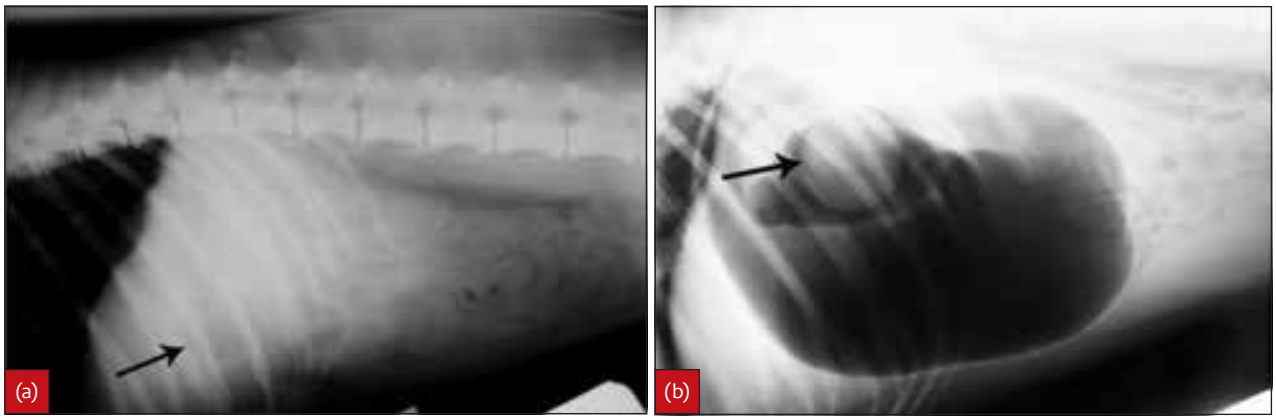
1. The patient should be conscious, not under general anaesthesia.
2. Administer orally 5–40 ml liquid barium sulphate, depending on the size of the patient and the site and nature of the lesion suspected. Alternatively, barium may be mixed with food and the animal allowed to eat this naturally. This technique may be used to demonstrate a partial oesophageal obstruction or to fill a distended oesophagus completely.
3. Take lateral radiographs of the neck and thorax 2–3 minutes after administration. A ventrodorsal or dorsoventral view is occasionally helpful. If contrast medium is retained, further radiographs may be useful to show its subsequent progress.

24.29 Procedure for an oesophageal contrast study.

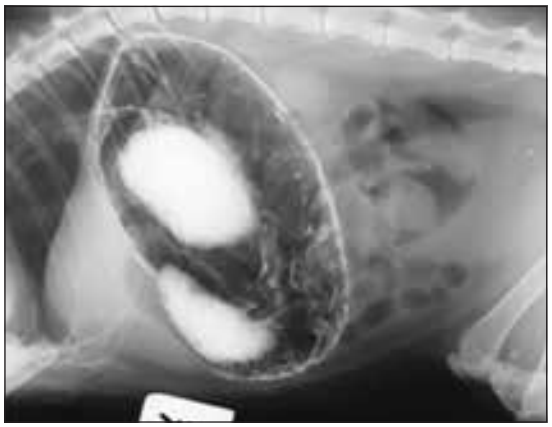
Gastrointestinal contrast studies

These have now largely been superseded by ultrasonography and endoscopy. However, they may still be useful for regions of the small intestine not accessible to endoscopy, and when ultrasonographic examination is inconclusive (Figures 24.30 and 24.31).

- Preparation of the patient is important in order to ensure that the stomach is empty and the colon contains minimal faecal material. Food and faeces will result in filling defects in the contrast column or pool, and thus mimic foreign bodies or masses.
- General anaesthesia should not be used, as it interferes with gastrointestinal motility and increases the risk of aspiration of contrast media.



24.30 (a) Right lateral view and (b) pneumogastrogram of a skeletally immature dog with a history of chronic vomiting. On the (a) survey film, a poorly defined region of lucency is visible in the region of the gastric pylorus (arrowed). The lesion appears rounded but is difficult to identify definitively. (b) After insufflation of the stomach with air, the gastric foreign body (rubber ball) is easily identified (arrowed).



24.31 Right lateral radiograph of a dog that has undergone a low-dose double contrast gastrogram. The stomach appears normal.
(Courtesy of Elizabeth Baines, Willows Referral Service)

- Water-soluble iodinated contrast media may be used in cases of suspected perforation. Arguments for and against their use are outlined in the section on oesophageal contrast studies. The hyperosmolarity of ionic iodinated contrast media tends to draw fluid into the lumen of the gastrointestinal tract, resulting in progressive dilution of the contrast and exacerbation of any existing dehydration.
- It is possible to evaluate the large intestine by following the barium through from the stomach. If a large intestinal lesion is specifically suspected, it may be quicker and more efficient to perform a barium enema instead, although endoscopy is usually the technique of choice in such situations.
- Normally, contrast begins to leave the stomach within 30 minutes but may be delayed up to 1 hour in nervous animals. Emptying of the stomach is usually complete within 4–6 hours. A delay in gastric emptying may occur due to ileus in the presence of systemic illness (e.g. renal failure, peritonitis), with the administration of certain drugs (e.g. opioids) or due to gastric outflow obstruction. In most animals, the time between onset of gastric emptying and appearance of barium in the large intestine is between 30 minutes and 1 hour, although this is very variable. Delayed intestinal transit may result from systemic illness, or from paralytic or obstructive ileus.
- Check the contrast pool or column for persistent filling defects, which may represent foreign material or masses projecting into the lumen. Since an apparent defect may be caused by a peristaltic or segmental contraction, it is important to be able to demonstrate that an abnormality is consistently found on successive radiographs.
- Evaluate the walls of the gastrointestinal tract for persistent areas of thickening or irregularity.
- Check for evidence of perforation and consequent barium leakage.

A procedure for upper gastrointestinal contrast studies is given in Figure 24.32.

1. Withhold food overnight, but allow the patient access to water. Administer an enema or allow the animal an opportunity to evacuate the bowel naturally before beginning the procedure.
2. The patient should be conscious or lightly sedated.
3. Administer 1–2 ml/kg liquid barium sulphate (the higher dose rate for smaller animals) either orally or by stomach tube.
4. Take a lateral view immediately, centred on the cranial abdomen, followed by a ventrodorsal view of the same area.
5. If a gastric lesion is suspected, additional views should be taken at approximately 15 and 30 minutes. If anything suspicious is seen (e.g. a filling defect or an area of irregularity), the same view should be repeated as soon as possible to confirm or rule out the suspected problem. It can be useful in some cases to take four views of the stomach (right lateral recumbency, left lateral recumbency, ventrodorsal and dorsoventral) as the barium and any gas in the stomach will occupy different parts of the stomach in each view.
6. For the small intestine, radiographs should be taken at 30 minutes and thereafter at hourly intervals until a lesion is seen or passage of barium into the colon has been demonstrated and the stomach is empty.

24.32 Procedure for an upper gastrointestinal contrast study.

Upper urinary tract contrast studies

- These studies are best carried out under general anaesthesia unless this is clinically contraindicated, as the intravenous administration of the contrast material may result in nausea or vomiting.
- A VD view of the abdomen immediately after injection of the contrast agent should show opacification of the renal parenchyma (Figure 24.33). A complete lack of opacification on this and subsequent radiographs may reflect disruption of the renal blood supply or a non-functional kidney. If the kidneys are opacified, then their size, shape and position should be evaluated.



24.33 Ventrodorsal abdominal view after intravenous contrast administration (intravenous urogram). This image shows a normal nephrogram phase. The kidneys are easily identified.

- After about 5 minutes, excretion of the contrast agent should be apparent, with contrast visible in the renal pelvis and ureter on each side (Figure 24.34). 'Renal shutdown' is a recognized but uncommon idiosyncratic reaction to the contrast medium, resulting in initial renal opacification but no visible excretion. Excretion usually begins a short while after administration of intravenous fluids and diuretics, and the animal should be treated for acute kidney injury (see Chapter 8). Other reasons for delayed visualization of the renal pelvis include pelvic/ureteral dilatation or obstruction, or severely impaired renal function.



24.34 Ventrodorsal abdominal view after intravenous contrast administration (intravenous urogram). This image shows a normal ureterogram phase. The kidneys, renal pelves and ureters are easily identified.

- Once excretion of the contrast agent is apparent, any distension of, or filling defects within, the ureters can be seen. Loss of integrity of a ureter with consequent spillage of contrast medium into the retroperitoneal space may be seen. Occasionally, the ureters may be seen to be intact but displaced by a mass or haemorrhage within the retroperitoneal space.

A procedure for intravenous urography is given in Figure 24.35.

1. Except in an emergency, withhold food overnight but allow the patient access to water. Administer an enema and wait for evacuation of the bowels before premedication.
2. Use general anaesthesia unless clinically contraindicated.
3. If the distal ureters are to be examined, catheterize the bladder to empty it of urine and introduce air before administering the contrast medium.
4. Use water-soluble iodinated contrast medium with a high iodine concentration (ideally 300–450 mg/ml). Administer 1 ml/kg contrast medium intravenously as a bolus.
5. For optimum delineation of the kidneys, take a ventrodorsal view of the abdomen centred over the kidneys immediately after injection of the contrast medium. A ventrodorsal view 5 minutes later will show opacification of the renal pelvis and ureter on each side.
6. Further views centred on the areas of interest are taken as and when required, depending on the indications for the examination. Excretion normally continues for at least 1 hour, and bladder filling may be seen 10–15 minutes after the intravenous injection. If renal function is grossly impaired, opacification of the renal pelvis and ureter may not occur or may be delayed for several hours. For examination of the distal ureters and the vesico-ureteric junction, oblique views of the pelvic area may be helpful in addition to the standard lateral and ventrodorsal views.

24.35 Procedure for intravenous urography.

Lower urinary tract contrast studies

- It is preferable to ensure that the colon and rectum are empty before beginning lower urinary tract contrast procedures, as faecal material may compress and obscure the bladder and prostate. If possible, catheterize and empty the bladder once survey radiographs have been taken.
- A positive contrast urethrogram (in the male) or vaginourethrogram (in the female) should allow evaluation of virtually the entire length of the urethra (Figure 24.36). Check for any irregularity of the urethral wall (e.g. due to neoplasia, inflammation or stricture formation), filling defects within the contrast column (e.g. due to calculi, blood clots, or masses; Figure 24.37), or leakage of contrast into the surrounding soft tissues (Figure 24.38). In the male dog, the path of the urethra through the prostate gland should be assessed, as an asymmetrical path is suggestive of focal prostatic disease (e.g. neoplasia, abscessation, cysts).
- Cystography allows evaluation of the bladder wall and lumen. If bladder rupture is suspected, positive contrast cystography is the preferred technique. Otherwise, double contrast cystography allows accurate assessment of the wall for thickening and irregularity and of free structures within the lumen, such as calculi or blood clots (Figure 24.39).

- Encourage normal evacuation of the bowel or administer an enema.
- General anaesthesia is generally required except in very sick or placid animals.
- It is not necessary to catheterize and empty the bladder unless intending to proceed on to cystography.
- **Urethrography**
  - For a male dog, take a small balloon catheter and prefill the catheter with water-soluble iodinated contrast medium. Introduce the catheter into the distal penile urethra and gently inflate the balloon to hold it in place.
  - Position the dog in lateral recumbency with both hindlegs drawn well forward.
  - Inject 5–20 ml of contrast medium via the catheter. Ensure radiation safety by wearing appropriate protective clothing and standing as far as possible from the primary X-ray beam.
  - Towards the end of the injection of contrast medium, take a lateral radiograph, including the caudal abdomen, pelvis and perineum.
  - The technique in the male cat is similar, but it is not possible to use a balloon catheter. Instead, introduce a plain catheter a couple of millimetres into the urethra and hold in place with a clamp across the prepuce. A volume of 2–3 ml of contrast medium is usually ample.
  - In males and females, dogs and cats, an alternative approach is to introduce the catheter just as far as the bladder. Estimate the approximate expected length of the urethra. Begin injecting contrast medium and, at the same time, steadily withdraw the catheter. Obtain the radiograph when it is judged that the catheter has been withdrawn sufficiently so that the tip of the catheter lies just in the distal urethra.
- **Vaginourethrography**
  - For a bitch, prefill a balloon catheter with water-soluble iodinated contrast medium.
  - Place the tip of the balloon catheter inside the vulva and inflate the balloon. Place tissue forceps to hold the vulva closed dorsal and ventral to the catheter, then gently pull the catheter back until the inflated balloon lies just in the vulva.
  - Inject contrast medium at a dose rate of approximately 1 ml/kg bodyweight. Ensure radiation safety by wearing appropriate protective clothing and standing as far as possible from the primary X-ray beam.
  - Towards the end of the injection, take a lateral radiograph, including the caudal abdomen and pelvis.
  - The technique is similar in the queen, except that it is necessary to use a plain catheter rather than a balloon type, held in place with a clamp across the vulva.
  - The contrast medium will usually fill the vagina first and then the urethra. Therefore, incomplete filling of the urethra may indicate an inadequate volume of contrast medium, leakage of contrast medium back around the catheter, or an animal at or around the time of oestrus.

Cystography

1. Encourage normal evacuation of the bowel or administer an enema.
2. General anaesthesia is usually required except in very sick or placid animals.
3. Catheterize and empty the bladder.

4a. Positive contrast cystography: inject 10–50 ml water-soluble iodinated contrast medium through the urinary catheter – a high level of iodine is not essential for this technique. Withdraw the catheter.

4b. Double contrast cystography: following a positive contrast cystogram, aspirate as much of the contrast medium as possible. Inject 30–200 ml of air according to the size of the animal. Inject the air until moderate resistance to injection is felt, or until distension of the bladder is felt on palpation of the caudal abdomen. Withdraw the catheter.

5. Take a lateral radiograph of the caudal abdomen as soon as possible after introduction of the contrast medium. Ventrodorsal and oblique views may be useful on occasions.

24.36 Retrograde urethrography, vaginourethrography and cystography.



24.37 Retrograde urethrogram in a dog with dysuria and haematuria. There is a filling defect in the prostatic urethra. The defect is irregular in margination. The prostate gland is moderately enlarged. Prostatic wash confirmed prostatic carcinoma.



24.38 Retrograde urethrogram of a cat that has recently suffered road traffic trauma. There is marked extravasation of contrast medium into the peri-urethral soft tissues, indicating urethral perforation.



24.39 Double contrast cystogram in a dog with haematuria. Several filling defects are present in the contrast puddle within the bladder. These structures are rounded in margination and vary in size. The ventral bladder wall is thickened. Radiological diagnosis: cystic urolithiasis and cystitis.

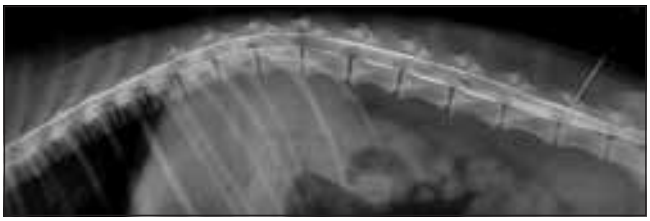
Spinal contrast studies

If available, MRI/CT may be preferred to spinal contrast studies (see below).

- General anaesthesia is mandatory for such procedures.
- It is important that only non-ionic water-soluble iodinated contrast media are used. The ionic media must not be used.
- Plan the procedure carefully before beginning, deciding on the preferred site of puncture and the required dose of contrast medium. These decisions will be influenced not only by the site of the suspected lesion, but the probable stability (or otherwise) of the vertebrae in the region.

- Once the contrast has been injected, follow its path from the site of injection to the region of interest, looking carefully for deviation or thinning of the contrast columns, which may allow localization of any spinal cord compression and differentiation between extradural, intramedullary and extramedullary/intradural lesions. Once a lesion has been identified, it is important to take radiographs in at least two planes (usually lateral and VD; Figure 24.40).

A procedure for spinal contrast studies (myelography) is given in Figure 24.41. Spinal contrast studies are rarely performed in primary emergency practice. Consideration should be given as to whether the expertise is available to do the study and also to act on any diagnosis subsequently made.



24.40 Lateral radiograph of the thoracolumbar spine of a dog that has sustained trauma after being hit by a car. The neurological localization was T3–L3. A myelogram has been performed. There is collapse of the T13–L1 intervertebral disc space and mild subluxation of T13–L1, with dorsal subluxation of the caudal aspect of T13 compared with L1. There is compression of both the dorsal and ventral contrast columns, confirming extradural cord compression secondary to the subluxation. (Courtesy of P Mahoney)

1. General anaesthesia is essential.
2. A water-soluble non-ionic iodinated contrast medium should be selected and warmed to approximately body temperature.
3. Dosage of the contrast medium will depend on both the size of the animal and the level of the suspected lesion. A dose rate of 0.3 ml/kg up to a maximum of 10 ml has been suggested, but this should be reduced if the suspected lesion is close to the site of injection.
4. Cisternal puncture: place the animal in lateral recumbency. Clip the puncture site and prepare aseptically. With the head flexed and held steady by an assistant, palpate the occipital crest and the two wings of the atlas. Place a sterile spinal needle, with the bevel facing caudally, perpendicular to the skin on the midline in the centre of the triangle formed by these landmarks. Advance the needle slowly until a 'pop' is felt as the needle enters the cisterna magna. Withdraw the stylet and wait for the flow of cerebrospinal fluid (CSF), which indicates correct needle placement. If the fluid is bloody, then withdraw the needle and repeat the procedure with a clean needle.
5. Lumbar puncture: the animal may be placed in either lateral or ventral recumbency, and the puncture site clipped and prepared aseptically. Palpate the dorsal spinous processes of the caudal lumbar vertebrae. Introduce a spinal needle on the midline, just in front of the dorsal spinous process of L6. Slowly advance the needle until it impinges on bone, then slowly 'walk' the tip of the needle forward along the bone until it passes through the intervertebral space. The needle passes for a short distance, coming to a stop on the floor of the spinal canal. Often a twitch of the hindlimbs or tail is noted as the needle passes through the cauda equina. CSF is not invariably obtained, even if the needle is correctly located, so a test injection of contrast medium may be required to check the position of the needle tip.
6. Inject the required dose of contrast medium slowly then withdraw the needle.
7. Following contrast medium injection, lateral radiographs are taken, starting at the site of the injection, and working progressively down (in the case of a cisternal injection) or up (in the case of a lumbar injection) the spinal column to follow the flow of contrast medium. If it fails to flow, then it may help to tilt the animal head up (if the contrast was given cisternally), or to apply traction to the spinal column. If a lesion is found, then a ventrodorsal view of the region should also be taken.

24.41 General procedure for performing myelography.

Ultrasonography

Diagnostic ultrasonography is an imaging technique that is a very useful complement to radiography. Ultrasonography is a safe, non-invasive technique which produces cross-sectional images of the soft tissues of the body. Information regarding the internal architecture of organs may therefore be obtained. In addition, these images are dynamic, so that movement of structures may be seen. Consequently, ultrasound examination is an extremely valuable imaging tool in critical patients. Furthermore, the patient can usually be allowed to adopt a comfortable position with minimal restraint during ultrasonographic examination. This is particularly helpful in critically ill and injured animals that may be in an unstable or fragile state.

Ultrasonography does, however, have limitations. The ultrasound beam is effectively blocked by bone or gas, so that the information gleaned from imaging skeletal structures, or gas-filled organs such as the lung or, on occasions, the gastrointestinal tract, is often minimal.

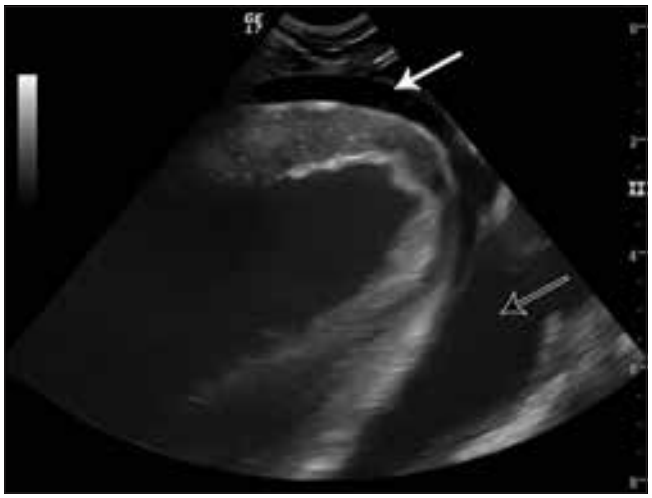
It may be useful to bear in mind the following principles when planning an ultrasonographic examination:

- Select the scanning site carefully by choosing an area of the body surface overlying the organ or tissue of interest, but avoiding intervening bone or gas
- Clip hair from the skin of the scanning site, clean the skin carefully and apply liberal quantities of acoustic gel to ensure good acoustic contact
- When a choice is available, select as high a frequency of sound as you can while still achieving an adequate depth of tissue penetration. In general, high-frequency sound (e.g. 7.5 MHz) will not penetrate as deeply, but will provide better image resolution than lower-frequency sound (e.g. 5 MHz)
- Once an image is obtained, optimize the detail by adjustment of gain controls, such that there is an even brightness throughout the depth of the image. Too dark an image will result in loss of visible detail, whereas too bright an image may obscure detail with background 'noise'
- Ensure that a thorough ultrasonographic examination is carried out, sweeping the sound beam through the entire area of interest, in at least two planes of section
- Colour flow and spectral Doppler techniques may be useful in some cases in order to define blood flow (in terms of direction, nature and velocity) within the cardiac chambers and great vessels.

Thorax

Other than to confirm the presence of pleural or pericardial fluid, the most common reason for a detailed ultrasonographic examination of the thoracic cavity is to evaluate the heart. While radiography enables an assessment of the shape and size of the cardiac silhouette only, ultrasonography will allow visualization of the separate chambers, great vessels and valves. For a full description of the recommended protocol for echocardiography, and the abnormalities which may be found, see the References and further reading (more information can also be found in Chapter 6). However, the following points may be helpful in assessing the critical patient:

- Pericardial fluid appears as an anechoic (black) band around the heart (Figure 24.42). It is important to evaluate the regions of the heart base and the right atrium carefully for evidence of hypoechoic (grey)



24.42 Thoracic ultrasonogram of a dog with dyspnoea. The left ventricle is visible from this apical view. There is a small volume of pericardial effusion (white arrow) and a moderate volume of pleural effusion (black arrow). A small mass was identified in the atrioventricular septum.



24.43 Right parasternal short-axis view of the heart at the level of the left atrium of a dog with a soft nocturnal cough and exercise intolerance. There is marked enlargement of the left atrium (arrowed), which should be no more than 1.5 times the size of the aorta at the level of the aortic valve. This dog had severe mitral regurgitation secondary to myxomatous mitral valve disease.

masses, which when present are usually neoplastic and the underlying cause of the effusion. Collapse of the right atrial wall during systole is evidence of cardiac tamponade and is an indication for immediate drainage of the pericardial fluid

- The thickness of the myocardium should be assessed. The myocardium may be thickened as a physiological response to a cardiovascular abnormality (e.g. right ventricular hypertrophy in response to pulmonic stenosis) or as part of the primary disease process (e.g. hypertrophic cardiomyopathy)
- Chamber size should be evaluated. Ventricular dilatation may be seen as a consequence of volume overload (e.g. a left-to-right shunting ventricular septal defect will result in pulmonary overcirculation and dilatation of the left atrium and ventricle). Atrial dilatation may occur in response to pressure or volume overload (e.g. reduced ventricular compliance as in hypertrophic or restrictive cardiomyopathy; atrioventricular valve insufficiency). A right parasternal short-axis view of the base of the heart shows the left atrium adjacent to the aorta. An evaluation of the ratio of the diameters of the left atrium and aorta (normally around 1:1) gives a useful indication of atrial dilatation. A left atrium to aortic ratio of greater than 1.5:1 is considered abnormal (Figure 24.43)
- The leaflets of each of the major valves should be assessed. Thickening and irregularity of valve leaflets may be seen in congenital (valvular dysplasia) or acquired (endocardiosis, endocarditis) disease. An abnormal motion may also sometimes be seen (e.g. rupture of chordae tendinae)
- Myocardial contractility may also be evaluated. It is useful to view overall myocardial movement on both long- and short-axis sections, in order to detect regions of myocardium with abnormal or reduced movements. M mode measurements may then be made in an attempt to quantify contractility – a number of different measurements may be made, but the potential limitations of each should be appreciated. For a full discussion of this complex area see the References and further reading. Myocardial activity may be reduced (e.g. due to myocardial disease) or increased (e.g. in association with atrioventricular valve incompetence).

The remaining structures in the thoracic cavity are not usually visualized in the normal animal, as they are obscured by air-filled lung. Thoracic ultrasonography is, however, an extremely useful way to confirm the presence of pleural effusion prior to thoracocentesis in dyspnoeic patients when radiography is considered too high a risk. Also, the presence of pleural fluid will act as an acoustic window, outlining and separating thoracic structures. If sufficient fluid is present, the great vessels may be followed in the mediastinum, partially collapsed lung lobes can be recognized and any solid masses lying within the fluid identified. The fluid itself usually appears anechoic (black), although the presence of particulate matter, fibrin strands, gas bubbles or a highly cellular content may result in echoes swirling within the fluid.

Abdomen

The presence of peritoneal fluid, as in the thoracic cavity, enhances ultrasonographic visualization by outlining and separating structures. If only a small amount of fluid is present, it will tend to accumulate in dependent parts of the abdomen and is most easily visualized between liver lobes or around the cranial pole of the bladder. A systematic approach to identification of peritoneal fluid as part of the triage examination (known as a FAST (focused assessment with sonography for trauma) scan) is now a routine part of emergency practice; further details are found in Chapter 1.

Liver and spleen

It is preferable to fast the patient for 12 hours before imaging the liver, as a food-filled stomach will obscure part of the liver. It is acceptable to allow the patient to drink, as fluid within the stomach does not impair image quality and indeed may act as a useful landmark.

Evaluation of the hepatic and splenic parenchyma may reveal irregularity of the surface of the organ, and focal or diffuse disturbances of the parenchymal architecture. Such changes are usually indicative of disease, but are non-specific. For example, circumscribed nodules in the hepatic or splenic parenchyma may be neoplasia, hyperplasia, abscesses, infarcts, haematomas or granulomas. Equally, a normal ultrasonographic appearance does not

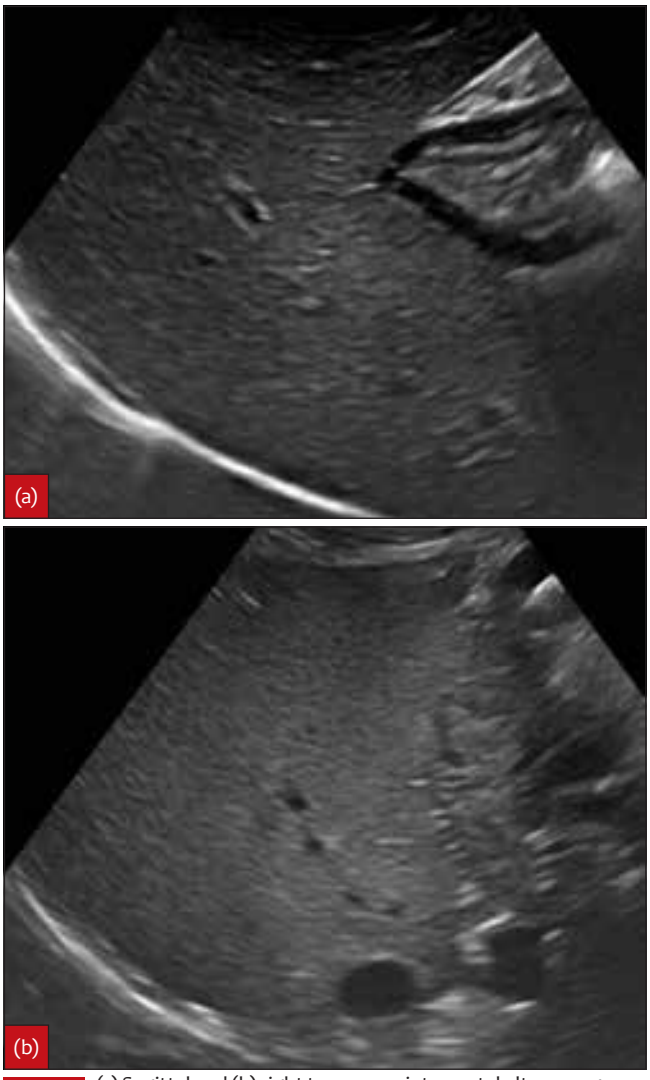
preclude disease. Therefore, a fine-needle aspirate or core biopsy tissue sample may be required for a definitive diagnosis (Figures 24.44–24.46).

The vascular supply can also be assessed. In the spleen, major vessels are visible only in the hilar region. In the liver, the caudal vena cava and portal veins can be identified, as well as their intrahepatic branches and tributaries. Thus, venous congestion can be recognized, as well as intraluminal thrombi or neoplastic invasion. Vascular anomalies, such as portosystemic shunts and arteriovenous fistulation, may also be recognized by the presence of single or multiple tortuous anomalous vessels.

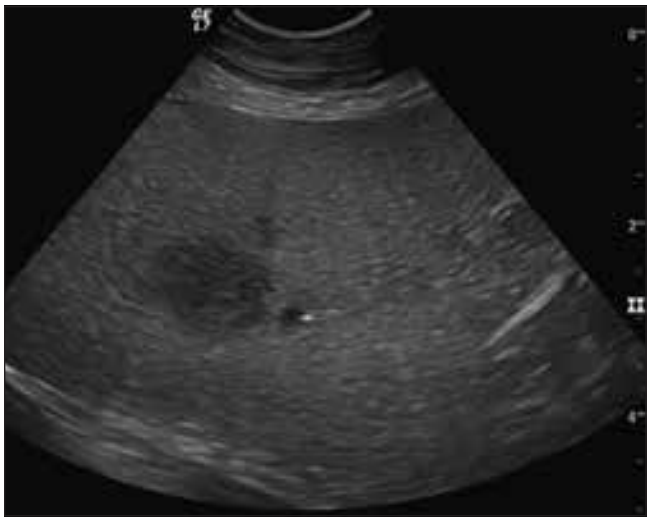
Within the liver, the gall bladder is readily seen, but the intrahepatic bile ducts are not usually visible. Distension of the common bile duct and subsequently the intrahepatic bile ducts can be detected in cases of obstructive jaundice.

Kidneys and adrenal glands

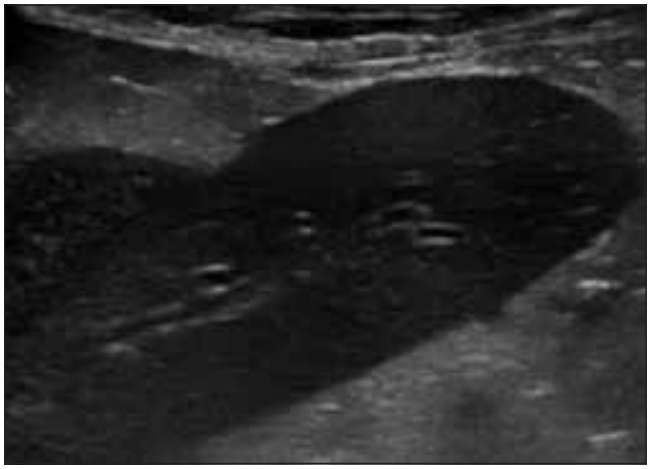
Ultrasonography provides a clear demonstration of the renal cortex, medulla and pelvis. Blurring or distortion of the normal architectural pattern indicates renal parenchymal disease but, once again, many of the changes seen are non-specific. In the critical patient, ultrasonography may be useful in differentiating between renal failure due to an acute renal insult or pre-renal causes, when the kidney often appears ultrasonographically normal, and renal failure due to established underlying renal disease, when ultrasonographic changes can often be seen (Figure 24.47).



24.44 (a) Sagittal and (b) right transverse intercostal ultrasonograms of a normal canine liver. The bright hyperechoic walled vessels are hepatic portal veins. The dark hypoechoic walled vessels are hepatic veins.



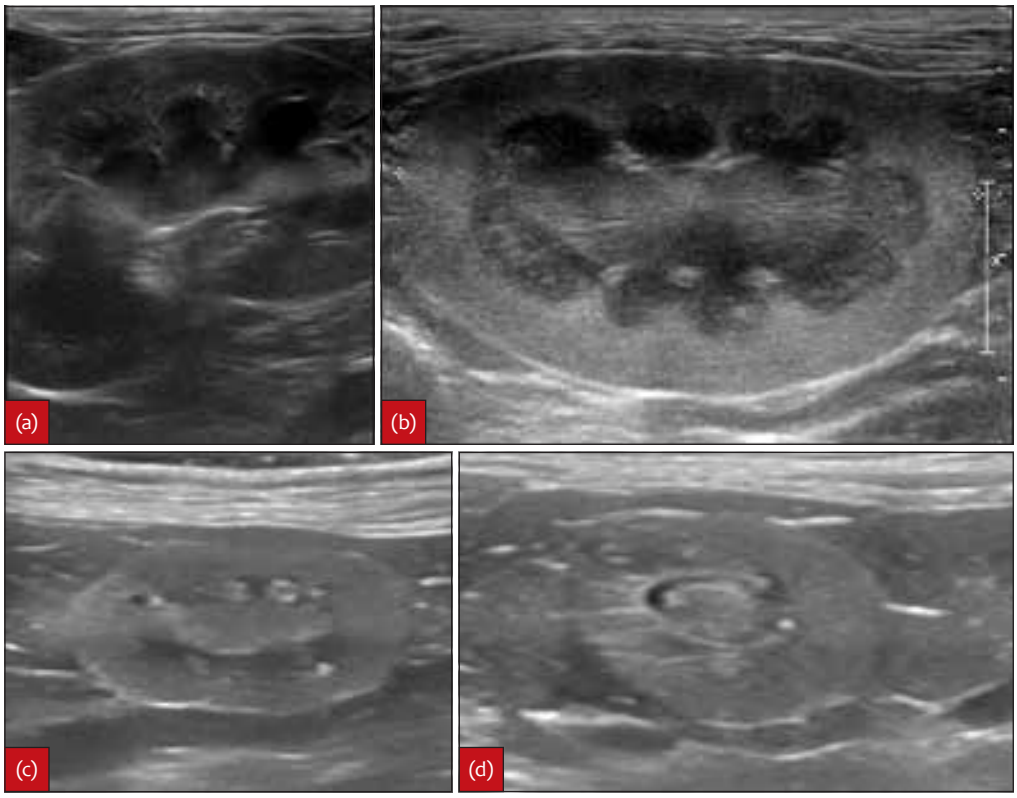
24.45 Ultrasonogram of the canine spleen. Note the fine echogenic texture (like fine sand). There is a poorly defined hypoechoic nodule within the splenic parenchyma. Fine-needle aspiration of the lesion revealed extramedullary haematopoiesis.



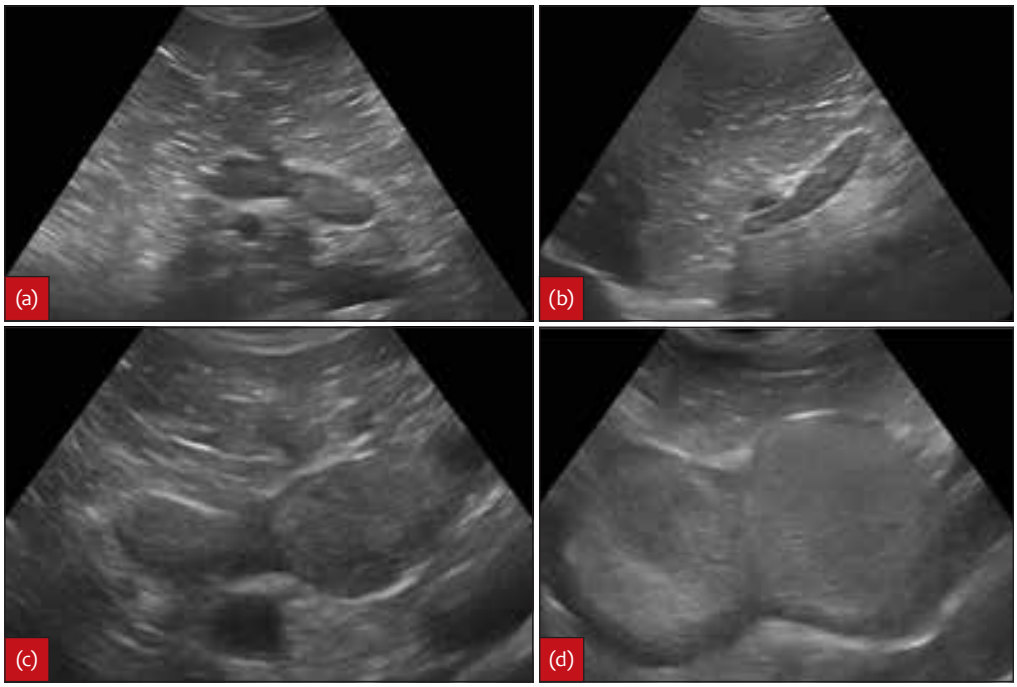
24.46 Ultrasonogram of the liver of a cat with icterus. The liver margins are rounded and there is evidence of hepatomegaly. The parenchyma is hypoechoic, with increased visualization of the hepatic portal veins. Histological diagnosis was amyloidosis.

Dilatation of the renal pelvis (e.g. due to ureteral obstruction or ascending urinary tract infection) is readily detected. Dilatation of the proximal ureter as it leaves the kidney and of the distal ureter as it approaches the bladder may be detected, but the middle section is often difficult to distinguish. Calculi may be identified in the renal pelvis or in the ureters.

The adrenal glands may be identified medial to the cranial pole of each kidney in close apposition to the aorta (left adrenal) or caudal vena cava (right adrenal), if the patient is not too obese (Figure 24.48). The adrenal glands are normally hypoechoic elongated structures. Enlargement of the gland, with loss of the normal elongated shape and even echotexture, may be seen with either adrenal hyperplasia or neoplasia. Remember to check the adjacent great vessels for evidence of invasion or thrombus formation if an adrenal mass is found.



24.47 (a–b) Longitudinal ultrasonograms of normal canine kidneys. (c) Longitudinal and (d) transverse ultrasonograms of a feline kidney with chronic tubulointerstitial nephritis (chronic kidney disease). The kidney is markedly reduced in size and appears hyperechoic. There is mild pyelectasia and loss of corticomedullary distinction.

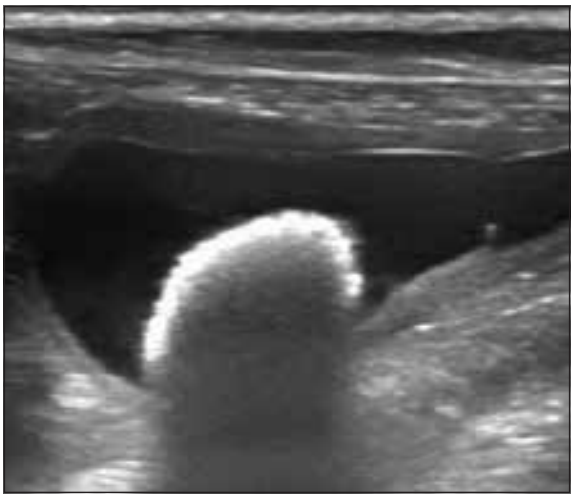


24.48 (a) Ultrasonogram of a normal left adrenal gland. Note the peanut shape.
(b) Ultrasonogram of a normal right adrenal gland.
(c) Ultrasonogram of a left adrenal gland. There is a heterogeneously isoechoic nodule in the caudal pole of the gland. The origin of this nodule is not clear from imaging alone and should be interpreted in the light of clinical findings, as these nodules are often incidental.
(d) Ultrasonogram of the left adrenal gland of a dog undergoing treatment with trilostane. The gland is markedly enlarged and has lost its normal shape. There is increased corticomedullary distinction. This is considered a normal finding in dogs treated with trilostane.

Bladder and prostate gland

Ultrasonographic examination of the bladder allows careful evaluation of the wall for regions of thickening or irregularity or for discrete masses projecting into the lumen. It may be helpful for treatment planning to determine the precise location of any mass relative to the bladder neck and the points of entry of the ureters, as well as the size of the mass. It is difficult to differentiate between a polypoid or neoplastic mass and a blood clot adherent to the bladder wall. Sequential examinations over a period of time may be required to clarify the situation. Calculi, irrespective of their mineral composition, are seen as echogenic structures lying in the dependent part of the bladder (Figure 24.49). Hypoechoic masses floating freely within the lumen of the bladder are likely to be blood clots.

The prostate gland is located caudal to the bladder and may be predominantly intra-abdominal or intrapelvic in location. It should be smooth in outline, with an evenly granular hypoechoic appearance. Small fluid foci measuring <1 cm in diameter are considered normal findings.



24.49 Longitudinal ultrasonogram of the bladder of a dog with intermittent haematuria and dysuria. There is a large lesion (a calculus) within the lumen of the bladder that is characterized by a hyperechoic proximal interface and long distal acoustic shadows.

Larger fluid foci may represent intraprostatic cysts, haematocysts, abscesses or tumours with necrotic centres. Disturbance of the normal parenchymal architecture may occur as a result of either inflammatory or neoplastic disease. Therefore, fine-needle aspiration of fluid foci and tissue core biopsy of disturbed parenchyma may be necessary for a definitive diagnosis.

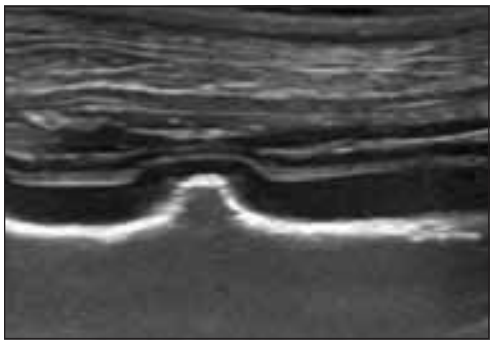
Uterus

Ultrasonography is the imaging modality of choice for differentiation between uterine enlargement due to pregnancy and that due to disease. From 3–4 weeks of gestation onwards, fetal structures may be clearly recognized within the uterus, and fetal viability assessed in terms of generalized fetal movements and fetal cardiac activity. Cessation of fetal movements and subsequent loss of fetal structure is indicative of fetal death. In the absence of fetal structures, accumulation of fluid within the uterus is abnormal and usually indicates pyometritis (see also Chapter 15).

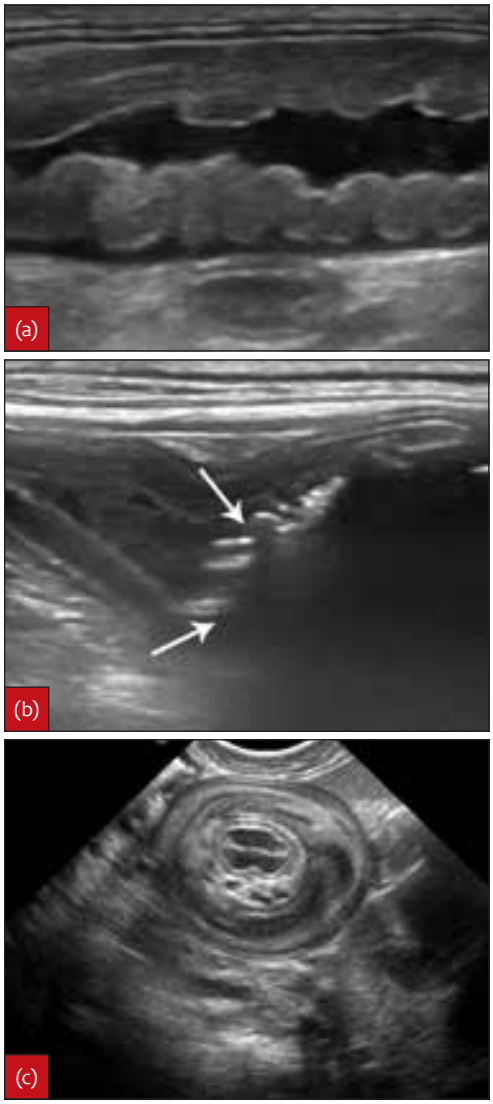
Gastrointestinal tract and pancreas

The gastrointestinal tract is amenable to ultrasonographic examination provided it does not contain excessive gas. If a high-frequency transducer is used to obtain images of optimal quality, then a distinct layered appearance of the wall of the stomach and small intestine is seen. The alternating hyperechoic and hypoechoic layers correspond exactly to the histological layers of mucosa, submucosa, muscularis and serosa (Figure 24.50). The lumen may be collapsed, with a central hyperechoic streak representing residual mucus and ingesta, or may be fluid filled. In the normal animal, peristaltic and segmental contractions can be seen.

Gross thickening of the wall may be detected, either with retention of the normal layered structure (usually hypertrophy or inflammation) or loss of normal architecture (severe inflammation or neoplasia). If abnormal fluid distension of the stomach or small intestinal loops is seen, it is useful to determine whether peristaltic and segmental contractions remain, or whether they are reduced or absent. If fluid is present within the gastrointestinal lumen, then foreign material or intraluminal masses may become evident (Figure 24.51). Intussusceptions also have a characteristic ultrasonographic appearance (Figure 24.51c).

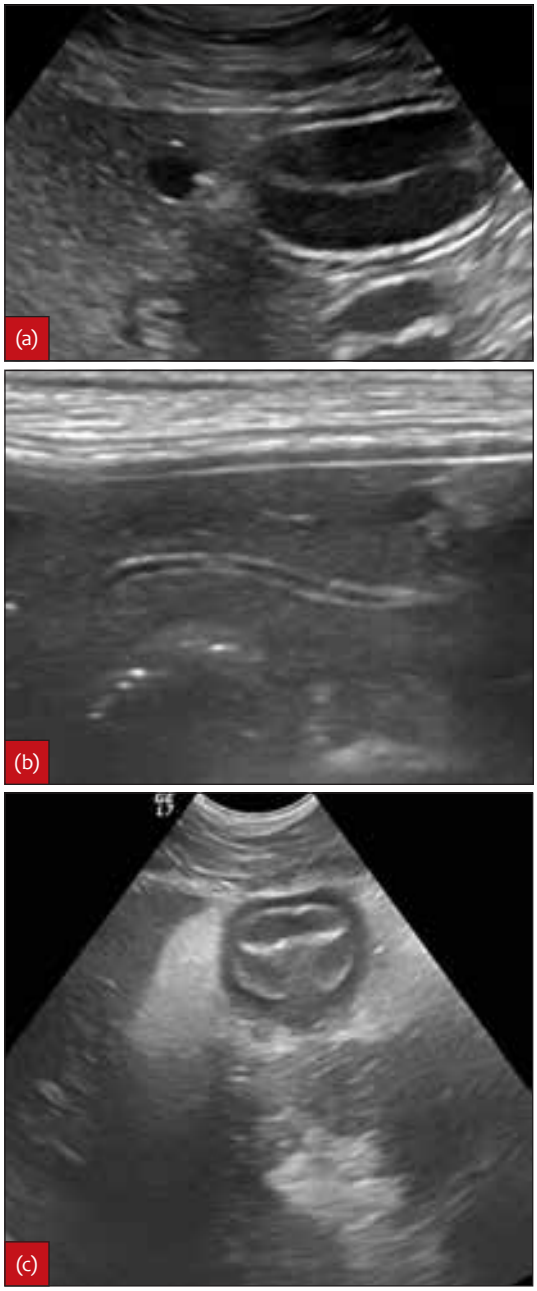


24.50 Longitudinal ultrasonogram of the duodenum, showing the normal appearance of a pseudoulcer (a region of thinned mucosa for antigen presentation). The normal intestinal wall layering is readily identified.



24.51 (a) Longitudinal ultrasonogram of the duodenum of a puppy with severe vomiting and diarrhoea. The intestinal wall is markedly thickened and the mucosa is markedly hyperechoic with a slightly corrugated appearance. Peristalsis was slow and static fluid was visualized within the lumen. Diagnosis: duodenitis. (b) Longitudinal ultrasonogram of the duodenum of a dog with acute vomiting. The duodenal lumen can be seen to widen around a large intraluminal mass characterized by a hyperechoic proximal interface and long distal acoustic shadows (arrowed). Diagnosis: duodenal foreign body. (c) Transverse ultrasonogram of a loop of jejunum of a vomiting puppy with a palpable abdominal mass. A normal loop of jejunum (intussusceptum) is identified surrounded by mildly dilated mesenteric blood vessels and fat, within another dilated loop of jejunum (intussuscipiens). Diagnosis: intussusception.

The pancreas is difficult to image ultrasonographically, partly because of its awkward location and partly because of its poorly defined margins (Figure 24.52). The right lobe of the pancreas lies in the right cranial quadrant of the abdomen closely apposed to the descending loop of the duodenum. In acute pancreatitis, the pancreas becomes enlarged, often with hypoechoic regions representing necrosis and haemorrhage (Figure 24.52c). The adjacent duodenum may be dilated and static, with a thickened wall. Peritoneal fluid and increased echogenicity of fat may also be noted in this region.



24.52 (a) Transverse ultrasonogram of the normal appearance of the canine pancreas (right lobe). The duodenum is to the right of the image. The pancreaticoduodenal vein is seen within the pancreas in cross-section. (b) Longitudinal ultrasonogram of the normal feline pancreas. The pancreaticoduodenal vein is identified in longitudinal section. (c) Transverse ultrasonogram of the canine pancreas (right limb). The pancreas is enlarged and heterogeneously hypoechoic. The surrounding mesenteric fat is heterogeneously hyperechoic. The duodenal wall is thickened. Diagnosis: acute pancreatitis, mesenteric steatitis and duodenitis.

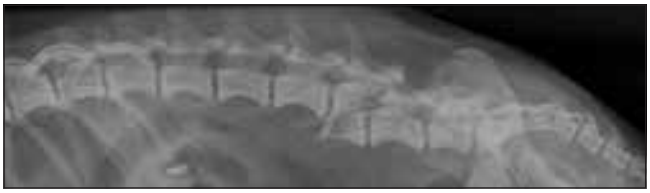
Computed tomography and magnetic resonance imaging

The neurological emergency

One of the first decisions to make when admitting the neurological emergency patient is whether the patient will benefit from immediate diagnostic imaging. However, it is imperative that the patient be fully assessed and have life-threatening injuries corrected as much as possible, so that it is stabilized prior to diagnostic imaging. Imaging will be pointless if all it tells you is why the patient just died. Of course, many cases may require imaging as part of their emergency work-up (e.g. cases with concurrent dyspnoea), but as a general rule, the patient should be fully assessed and stabilized as much as possible prior to imaging.

The use of CT or MRI often necessitates referral of the patient to a centre with the relevant imaging equipment, or waiting for the next local visit of a mobile MRI/CT imaging unit. Furthermore, general anaesthesia is always essential for MRI, and often required for CT despite the shorter scanning times achieved with modern equipment. This means that MRI and CT are unlikely to be used in the initial evaluation of a critical and unstable patient except in a few specialist centres. However, both techniques may provide valuable information once the patient has been stabilized.

Which modality to use will depend on a number of factors. Radiography has been described in detail above and can be considered the first line of investigation for the imaging emergency. Many spinal conditions, including discospondylitis, pathological fractures (e.g. secondary to neoplasia), congenital malformations and traumatic fractures (Figure 24.53) can be identified by radiography alone. It is also cheap and readily available, and will give images relatively quickly. Radiography allows imaging of the thorax and abdomen for patients with concurrent injuries (e.g. pneumothorax) or illness (eg. pulmonary metastases for cases with central nervous system (CNS) neoplasia). Dynamic studies (e.g. careful minimal flexion of the neck in cases with atlantoaxial subluxation or odontoid process fracture) are also possible. For spinal injuries, survey radiographs may be taken in the conscious patient, with more carefully positioned images taken afterwards, using sedation or general anaesthesia if required. Lastly, myelography may be used for cases with suspect spinal disease and compressive lesions. Disadvantages of radiography include the requirement for good technique, which is not always possible in conscious patients. For example, many spinal fractures will only be visible on one orthogonal view. Therefore, sedation or general anaesthesia may often be required. Due to its inferior soft tissue contrast (compared with other imaging modalities), radiography gives almost no information on brain injury or disease. There are a small number of exceptions to this



24.53 Lateral radiograph of a canine lumbar spine of a patient that has sustained road traffic trauma. The dog had no deep pain sensation. There is an oblique fracture through the vertebral body of L5 with displacement of the caudal segment cranioventrally. Clearly, advanced imaging is not required in this case, given the severity of the radiological and clinical findings.

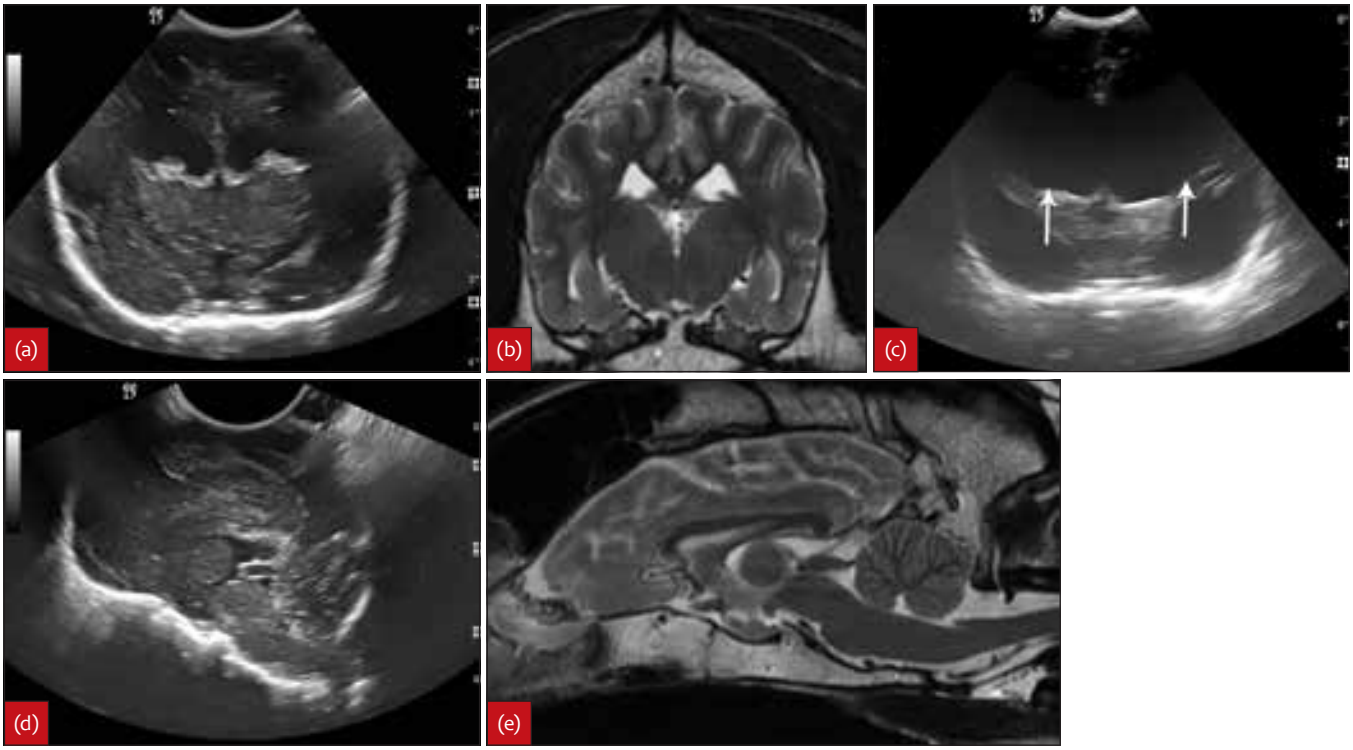
rule. For example, many meningiomas, particularly in cats, will cause sclerosis of the overlying calvarium, which may be visible on radiographs. Radiography also gives very little information on soft tissue paraspinal injuries. A further disadvantage is that myelography is an invasive technique and, as such, is not without risk. Lastly, radiography uses ionizing radiation (as does CT).

Ultrasonography requires little or no sedation and has the advantage of facilitating biopsy or fine-needle aspiration of lesions. It may also be used for examining peripheral nerves or nerve roots, although not strictly in the emergency situation. In animals with an open bregmatic fontanelle, thin calvarial bones or skull fractures that facilitate an acoustic window, gross structural brain disease (e.g. hydrocephalus) can also be ascertained (Figure 24.54). However, in most cases the thicker bone of the calvarium hinders acoustic penetration and so the modality is rendered useless.

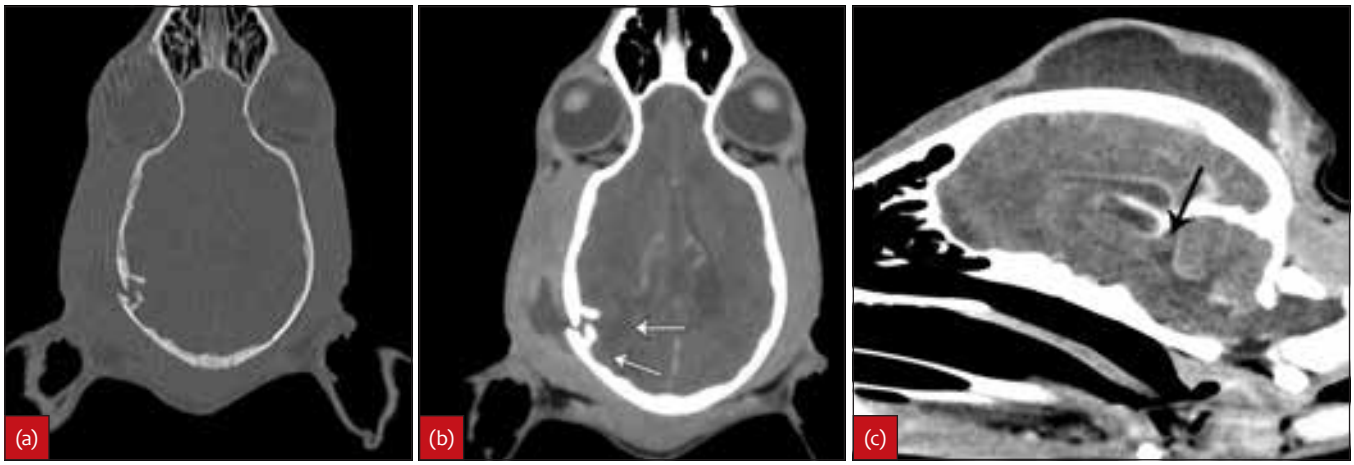
When assessing the patient for cross-sectional imaging, neurolocalization is important. For example, CT is less useful for injuries to the brain (although it can be used in cases where a rapid diagnosis of haemorrhage or raised intracranial pressure is required; Figure 24.55). MRI has much better soft tissue contrast for such cases. Availability of various advanced imaging modalities to the clinician will have an obvious impact on choice. The cost to the client is an important factor. Cross-sectional imaging is expensive and may therefore preclude its use. Imaging modality choice may also be affected by whether the patient will tolerate sedation or general anaesthesia, or whether conscious imaging is required. MRI requires general anaesthesia, whereas CT can be used in sedated or possibly conscious patients. It should be remembered that sedation and general anaesthesia will cause muscle relaxation and therefore the protective mechanism of muscle contraction for spinal injuries ('splinting') will be lost. Many emergency imagers would therefore recommend conscious radiography, as far as is possible, before the use of sedatives and general anaesthesia, to screen patients and rule out gross injuries to the vertebrae (see Figure 24.53).

Cross-sectional imaging techniques are now increasingly widely available to veterinary surgeons (veterinarians), and therefore warrant consideration for the emergency or critically ill patient. CT makes use of X-rays to produce detailed cross-sectional images of the patient, removing the superimposition that hinders conventional X-ray imaging. It is the technique of choice for bone. Initial images are usually acquired in the transverse plane, but may then be reconstructed to produce images in any plane (multiplanar reconstruction (MPR)), with three-dimensional reconstruction (volume rendering) also possible given appropriate software (Figure 24.56). After an image data set has been acquired by the scanner, an algorithm is applied to the data depending on the specific organs of interest. If bone detail is required, then a sharp (bone) algorithm is applied. If soft tissue detail is required, then a soft (or standard) algorithm may be applied. It is important to remember that this does not affect the original data set. Consequently, different algorithms may be applied at any time after the data set is obtained. Furthermore, the grey scale of the image can be manipulated by selection of window width and level, thus enhancing either bone or soft tissue detail (Figure 24.57).

CT is a quick modality, particularly for modern multidetector units, allowing most patients to be scanned under sedation, although general anaesthesia is occasionally required. CT demonstrates bone structures particularly well, but soft tissue structures can also be seen. It has superior soft tissue contrast to radiography and can be



24.54 (a) Transverse ultrasonogram of the brain of a normal puppy. The image is acquired through an open bregmatic fontanelle. Assessment for gross structural disease can be made. (b) T2-weighted transverse magnetic resonance (MR) image of a different dog at the same level. Clearly, the contrast resolution on MRI is substantially increased compared with ultrasonography. (c) Transverse ultrasonogram of the brain of a puppy through the bregmatic fontanelle. The lateral ventricles appear enlarged, presenting as large, paired, well demarcated anechoic structures (arrowed). The lateral recesses of the lateral ventricles also appear enlarged. Visible brain parenchyma is reduced in volume (compared with Figure 24.54a). (d) Sagittal ultrasonogram of the brain of a normal puppy through an open bregmatic fontanelle. (e) T2-weighted sagittal MR image of the brain of a different dog, for comparison with Figure 25.54d.



24.55 Computed tomography (CT) images. (a) Dorsal reformatted multiplanar reconstruction (MPR) image of the skull of a dog that has recently sustained trauma, viewed using a bone window and sharp algorithm. A comminuted, slightly depressed fracture of the right temporal bone is visible. (b) Dorsal reformatted MPR image of the skull of the same dog as in (a), viewed using a soft tissue window and soft algorithm after contrast administration. A hypoattenuating region is seen within the masticatory muscles and within the brain parenchyma, directly adjacent to the fracture (arrowed). There is a contralateral midline shift within the brain, suggesting brain swelling. The changes represent cerebral oedema secondary to trauma. (c) Sagittal post-contrast reformatted MPR image of a dog that presented obtunded with a dorsal soft tissue swelling. The dorsal soft tissue swelling is visible. It has non-contrast-enhancing contents surrounded by soft tissue that exhibits contrast enhancement. There is caudal subtentorial herniation at the level of the osseous tentorium cerebelli (arrowed). The cerebellum is displaced caudally and there is indentation of the rostral border of the cerebellum. There is also herniation of the cerebellar vermis at the level of the foramen magnum. These changes are indicative of raised intracranial pressure.

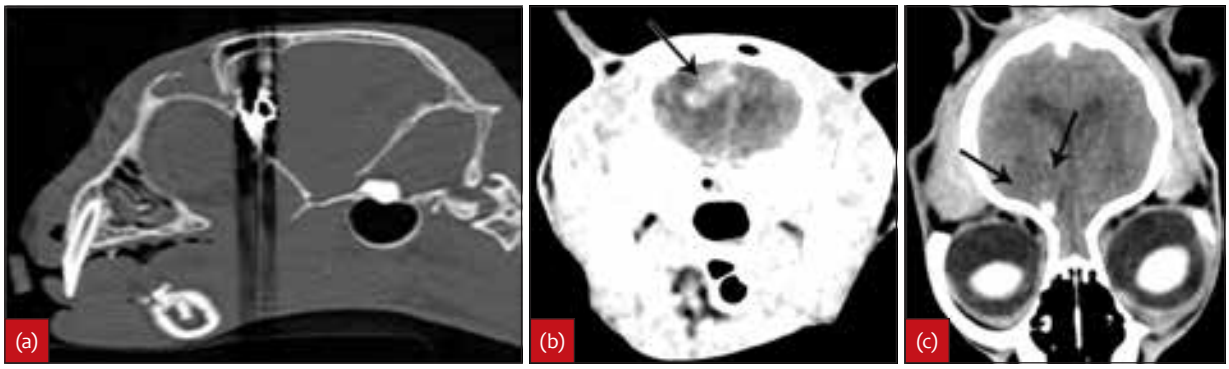


24.56 (a) Transverse and (b) dorsal multiplanar reconstruction (MPR), (c) oblique MPR and (d) surface-shaded volume-rendered images from a dog that had sustained head trauma after being kicked by a horse. Comminuted fractures involving the nasal cavity, frontal sinuses and orbits are visible. CT lends itself to this sort of orthopaedic detail.

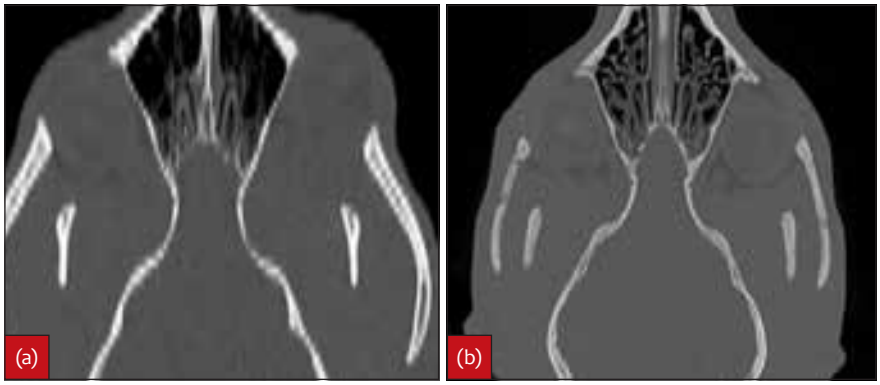


24.57 CT images: post-contrast transverse images of the skull of a dog that presented with left-sided facial swelling, pyrexia and seizures. (a) Bone window with a sharp algorithm. These display characteristics are most useful to assess bone detail. (b) Soft tissue window with a soft algorithm. These display characteristics are most useful to assess soft tissue injuries. (c) Brain window with a soft tissue algorithm. In this image, the brain can be assessed at the expense of other structures. There is a left temporal extradural abscess with associated increased intracranial pressure.

used for detecting disc injuries (either with or without iodinated intravenous contrast medium), as well as giving a substantial amount of information on possible concurrent thoracic or abdominal injuries. It can be used in conjunction with myelography to better assess compressive lesions. However, its soft tissue contrast is not as good as MRI, which would be the technique of choice for spinal cord injuries. A huge advantage of CT over MRI is that it can be used in cases where metallic fragments are present (e.g. ballistic injuries; Figure 24.58) or immediately after surgery where metallic surgical implants have been used. However, metal objects will undoubtedly degrade the image quality by causing beam hardening artefacts. Other beam hardening artefacts due to thick bone structures (e.g. the petrous temporal bone) may also hamper imaging (e.g. of the caudal fossa). Older, single-detector units may also suffer from stair step artefacts when performing MPR, due to the relatively thick slices acquired (Figure 24.59).

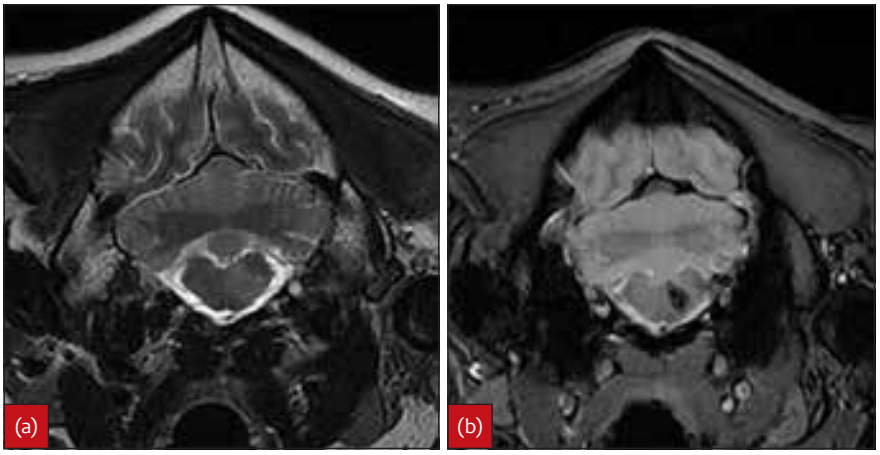


24.58 CT images. (a) Paramedian reformatted multiplanar reconstruction (MPR) image of the head of a cat that had been shot with an air gun, viewed using a sharp algorithm and bone window. The air gun pellet is visible surrounded by metallic beam hardening artefacts. However, it can still be identified within the frontal lobe. (b) Transverse image of the forebrain from the same cat as in (a) viewed with a soft tissue algorithm and brain window. Hyperattenuating material is seen within the dorsal right lateral aspect of the brain parenchyma (arrowed). This is compatible with intraparenchymal haemorrhage. (c) Dorsal reformatted MPR image of a dog that had sustained head trauma after being hit by a car. There is a midline shift of brain parenchyma to the left. A hyperattenuating lesion is present in the right rostral fossa, adjacent to the frontal bone. This represents a skull fracture. Around it, the brain parenchyma is hypoattenuating and enlarged, suggesting oedema (arrowed).



24.59 CT images. (a) Dorsal multiplanar reconstruction image of a normal canine cribriform plate. A stair step artefact is present secondary to non-isometric voxels. Effectively, this is an example of image under-sampling and poor spatial resolution. It is caused by the craniocaudal length of the image voxel being longer than the transverse dimensions and therefore the spatial resolution is much reduced when the image is rotated away from the transverse plane. It is commonplace in images from older single-slice CT units. (b) Similar image of a dog using isometric voxels. In this image, there is no reduction in spatial resolution caused by rotating the image from the transverse plane.

MRI uses a combination of radio waves and a powerful magnetic field allowing acquisition of cross-sectional images with exquisite soft tissue detail. Images may be obtained in any plane, and MPR is possible with 3D Fourier transform. It is undoubtedly the gold standard method for imaging brain, spinal cord and soft tissue injuries, but has poor bone contrast when compared with CT. It has the further advantage of being able to identify haemorrhage, particularly when using gradient echo sequences (e.g. T2*; Figure 24.60). Image contrast will depend on the spin-echo pulse sequence selected, and the relaxation properties of individual tissues. Image acquisition times are longer than with CT, so MRI examination is usually confined to the skull or spine, where respiratory movement is not an issue. The disadvantages of MRI include its large expense (both to the emergency clinic and consequently to the client) and the fact that it is time consuming. Unlike CT, where images are quick to obtain (especially with multidetector units) and can then be reconstructed in any plane (MPR), each imaging plane must be acquired separately. Image quality is also highly variable. This is due to the variation in equipment available (e.g. superconductor or open-field magnets, range of coils available) and also to the algorithms used in acquiring the images. This latter point makes a substantial difference to the diagnostic yield of the imaging study. Imaging very large or small dogs (and cats) may be difficult but is not usually impossible, although it may be considerably more time consuming. MRI cannot be used if mobile metallic fragments are present, or in dogs with pacemakers or other electronic devices.



24.60 Transverse MR images of the cerebellum and brainstem of a dog. (a) T2-weighted image. There is a poorly defined region of mildly increased T2-weighted hyperintensity within the left aspect of the mesencephalon. (b) Gradient recalled echo (GRE) T2*-weighted image. This image shows the region as a signal void (black). This is highly suggestive that the lesion is composed of haemorrhage. The dog was diagnosed with a coagulopathy secondary to angiostrongylosis.

Head

In patients with known or suspected head trauma, CT is probably the modality of choice. It is useful for complex calvarial fractures (see Figure 24.56), but gives limited information on specific CNS injuries. Whilst some information can be gained from CT about intracranial haemorrhage and CNS oedema (see Figure 24.58), MRI is more useful in these instances. However, MRI gives little detail of bone injuries.

In humans, extra-axial haemorrhage is well defined in CT imaging (Parizel *et al*., 2001). It may be divided into the following categories (Figure 24.61):

- **Epidural:** biconvex between the meninges and the periosteum. The haematoma does not cross suture lines but may cross the midline
- **Subdural:** crescent-shaped between the dura and the arachnoid mater. The haematoma does cross the suture lines but does not cross the midline
- **Subarachnoid:** blood mixes with cerebrospinal fluid (CSF) and basal cisterns.

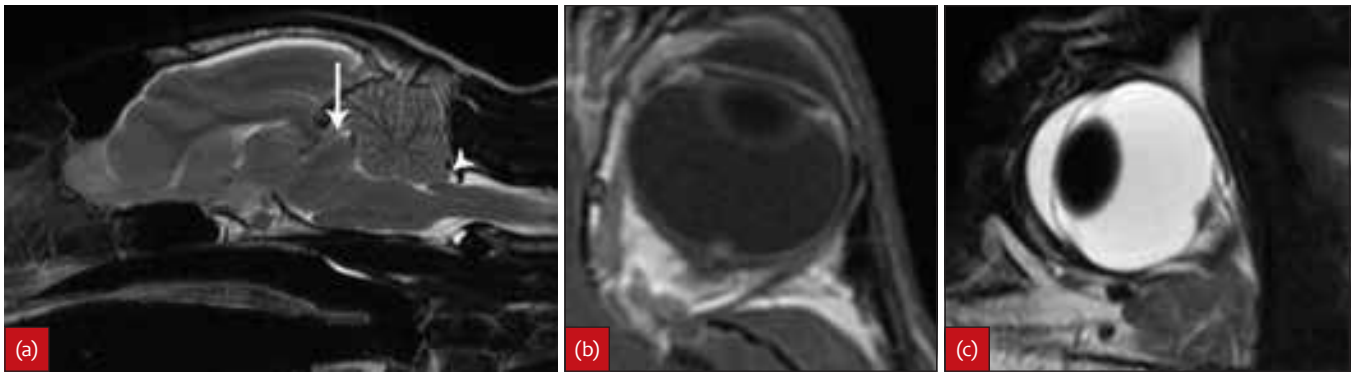
The appearance of the haematoma on CT will depend on atomic number and physical density. Large haematomas may exhibit the haematocrit effect, where layers containing sedimented cellular elements of blood and supernatant of plasma may be visible. Raised intracranial pressure can be the result of haemorrhage, haematoma and oedema, as well as depressed skull fractures and direct trauma. Inflammatory changes, such as those seen with penetrating injuries and concurrent empyema, will also cause increased intracranial pressure. Raised intracranial pressure can manifest as papilloedema, subtentorial, subfalcine or foramen magnum herniation (Figure 24.62), as well as herniation through a calvarial defect. These changes are readily identified on MRI, and often on CT.

Spine

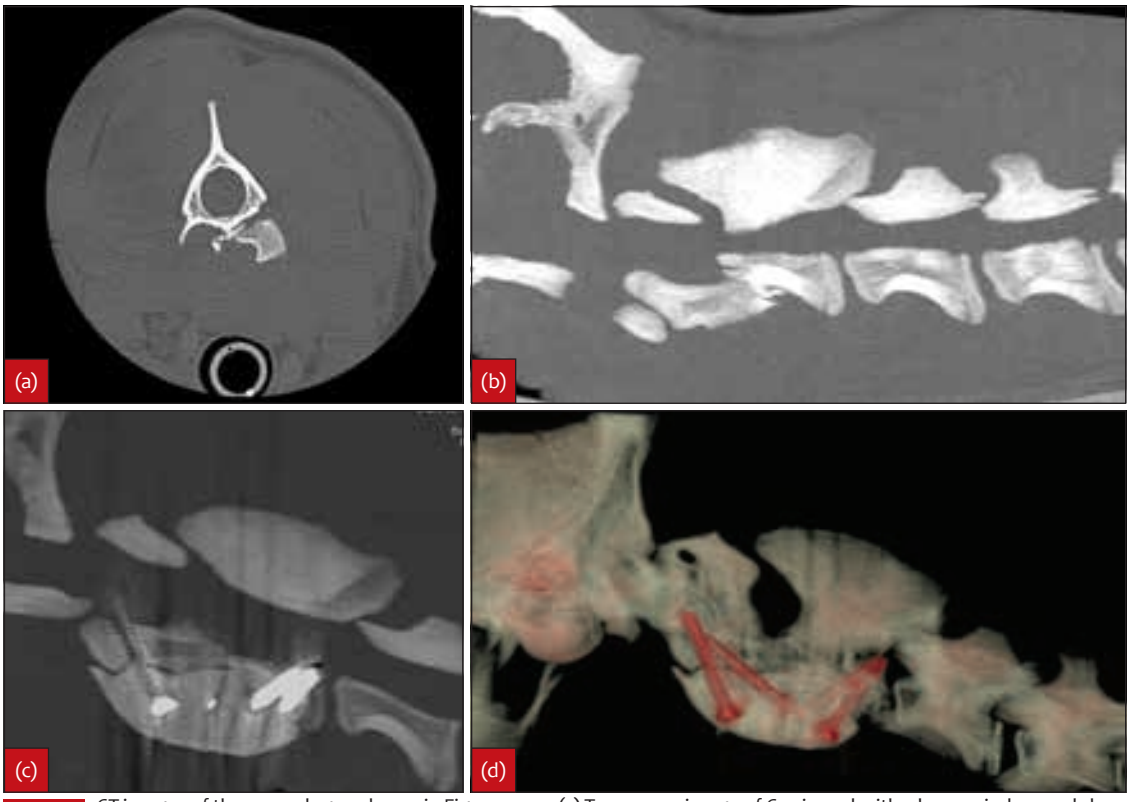
Vertebral fractures must be managed carefully in order to protect the spinal cord and nerve roots from further trauma. However, some spinal fractures may be visible only on well positioned X-ray studies, often involving anaesthesia or sedation. Chemical restraint, however, will remove the protective splinting of the surrounding musculature. Therefore, survey radiographs prior to chemical restraint are advisable. Radiography alone cannot be used to rule out potentially unstable spinal fractures, and CT is considered the modality of choice when such injuries are suspected (Kinns *et al*., 2006). MRI, however, has the added advantage of being able to assess damage to the cord, haemorrhage and changes to paraspinal soft tissues more accurately. CT offers the advantage of being able to assess postoperative images, even after metallic implants have been used, although as described previously the images will be degraded by artefacts. Some CT software can tell the difference between bone and metallic implants and represent them with moderate accuracy on 3D semi-transparent rendered images (Figure 24.63). Care should be taken to differentiate traumatic fractures from those that are pathological in nature.



24.61 Schematic diagrams representing transverse CT images of the forebrain and haemorrhage (red). (a) Epidural: biconvex between the meninges and the periosteum. The haematoma does not cross the suture lines but may cross the midline. (b) Subdural: crescent shape between the dura and the arachnoid mater. The haematoma does cross the suture lines but does not cross the midline. (c) Subarachnoid: blood mixes with cerebrospinal fluid and basal cisterns.
(Courtesy of CR Lamb, Royal Veterinary College)



24.62 MR images. (a) T2-weighted sagittal image of the brain of a cat with increased intracranial pressure. There is caudal displacement of the thalamus and mesencephalon caused by a rostral fossa mass (not shown). This causes caudal subtentorial (arrowed) and cerebellar (arrowhead) herniation. It is a poor prognostic indicator. (b) T1-weighted post-contrast and (c) T2-weighted images of the eye. There is a T1-weighted hyperintense, T2-weighted hypointense region of the caudal aspect of the eye that projects into the vitreous body. This is the optic disc and represents papilloedema. This is an indication of raised intracranial pressure.



24.63 CT images of the same dog as shown in Figure 24.27. (a) Transverse image of C2 viewed with a bone window and sharp algorithm. The fracture is clearly identified. (b) Thick-slice sagittally reformatted maximum intensity view of the cervical spine. This method of image display gives more information as to how the fracture fragments relate to each other. The short oblique vertebral body fracture of C2 is clearly visible. There is evidence of narrowing of the vertebral canal secondary to displacement of the caudal fracture fragment. (c) Thick-slice sagittally reformatted maximum intensity view after fracture reduction and surgical stabilization. The vertebral canal diameter has been normalized. Metallic artefacts are present secondary to implants. The screws are embedded in polymethyl methacrylate ventral to the vertebral body of C2. (d) Semi-transparent volume-rendered CT image of the same dog. In this image, the computer software recognizes metallic implants and displays them as a different colour to bone (red).

Intervertebral disc herniation is a common condition in the dog but is encountered less frequently in the cat (Figure 24.64). Whilst intervertebral disc protrusion and extrusion have been well described in the literature, low-volume, high-velocity disc injuries have also been identified (Chang *et al*., 2007). These lesions usually occur during strenuous activity and are thought to be due to supraphysiological forces acting on the intervertebral disc. These forces cause a small portion of healthy nucleus pulposus to split the annulus fibrosis and travel at some speed across the vertebral canal, causing spinal cord injury in the process. These injuries are only really identifiable on magnetic resonance imaging, as computed tomography lacks the contrast resolution required and lesions do not always cause changes in the spinal cord diameter.

On high-resolution images (for example, three-dimensional (3D) steady-state free precession and fast imaging employing steady-state acquisition (FIESTA) images), the hyperintense tract may be identified, and is often with associated mild extradural haemorrhage. These changes differentiate such injuries from the changes commonly identified with ischaemic myelopathy (Figure 24.65). Further intervertebral disease has more recently been identified (e.g. acute hydrated nucleus pulposus extrusion; Beltran *et al*., 2012).

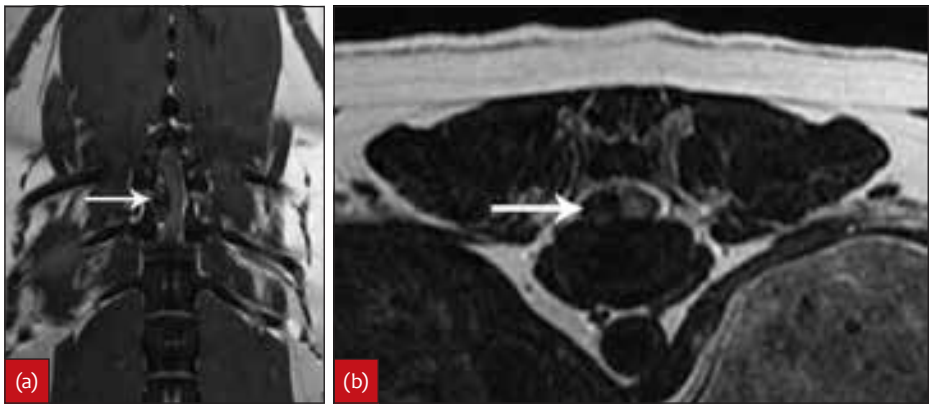
Lastly, the appearance of myelomalacia (haemorrhagic infarction of the spinal cord that can occur as a sequel to acute spinal cord injury; Platt *et al*., 2006) should be recognized, as this condition has potentially life-threatening consequences and a dramatic effect on prognosis (Figure 24.66).

Thorax

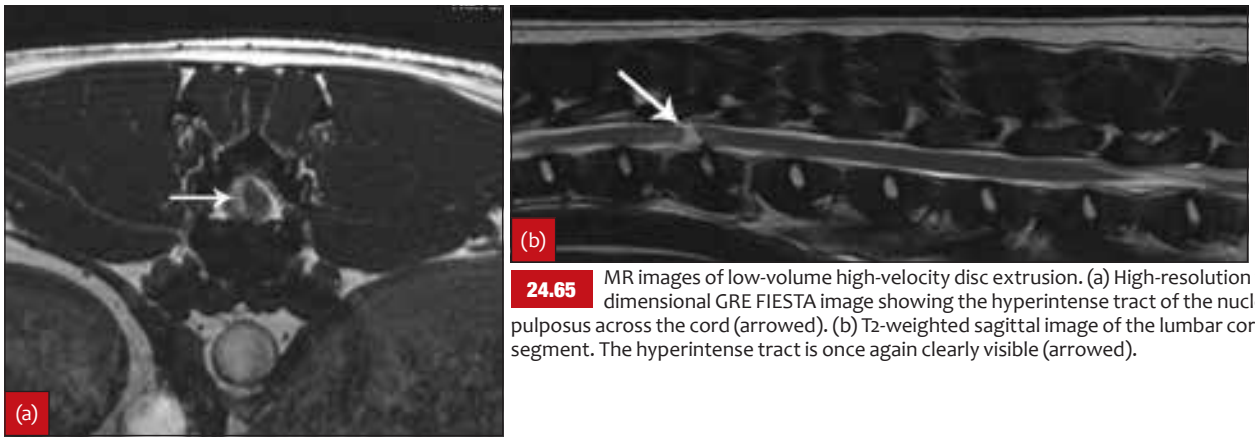
Increasingly, thoracic CT is being used in the emergency situation. It is probably most useful for those cases where the disease is complex or radiographic findings are ambiguous. Candidates should be stable enough for sedation or general anaesthesia. Proprietary constraint devices are available that allow patients to be confined, with inclusion of oxygen and intravenous fluid lines if required, if sedation or anaesthesia is deemed too hazardous. As multidetector CT units will allow isometric voxel acquisition (that is, a cube of scanned patient that has the same dimensions all round), then positioning in these patients is less of an issue than it used to be. Consequently, the data set can be viewed in any orientation. Occasionally, contrast techniques can be used for assessment of specific structures. In the thoracic emergency situation, arguably the most important of these is pulmonary angiography. By using bolus tracking techniques, the thorax can be scanned when contrast is visible within the pulmonary arterial tree, allowing assessment of vascular thromboses and occlusion of specific vessels (non-selective pulmonary angiography).

Abdomen

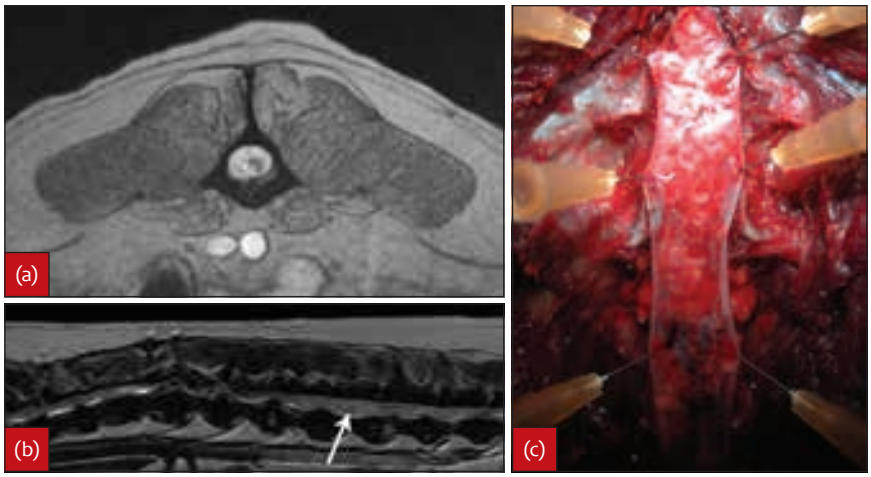
Typical abdominal CT candidates will be those that are not amenable to imaging via another technique. In reality, these will be large dogs where ultrasonography is not useful. These cases will require chemical restraint to obtain diagnostic images (Figure 24.67). Abdominal MRI is not, at present, useful for veterinary patients due to excessive respiratory motion and blood vessel-induced artefacts.



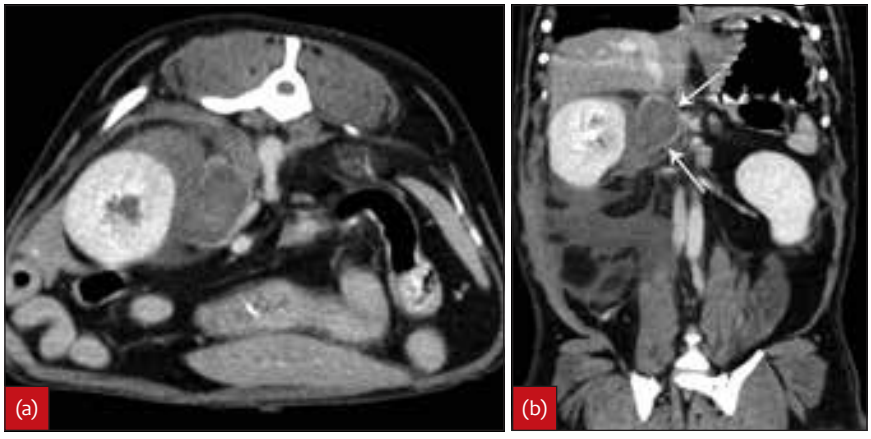
24.64 MR images of an intervertebral disc extrusion. (a) Three-dimensional dorsal gradient recalled echo (GRE) fast imaging employing steady-state acquisition (FIESTA) image of the spine of a dog that presented with neurological deficits that localized to the thoracolumbar spine. The image shows a heterogeneously hypointense, well demarcated extradural lesion at the level of the T11–12 intervertebral disc on the right (arrowed). The lesion caused moderate cord compression. (b) T2-weighted transverse image of the same dog as in (a). The extruded disc material presents as an extradural compressive lesion within the vertebral canal on the right of the cord, which is displaced to the left and moderately compressed (arrowed).



24.65 MR images of low-volume high-velocity disc extrusion. (a) High-resolution three-dimensional GRE FIESTA image showing the hyperintense tract of the nucleus pulposus across the cord (arrowed). (b) T2-weighted sagittal image of the lumbar cord segment. The hyperintense tract is once again clearly visible (arrowed).



24.66 MR images: myelomalacia. (a) Transverse GRE and (b) T2-weighted paramedian images of the lumbar spine of a dog with an intervertebral disc extrusion. There are regions of signal void (black) within the cord on the GRE image. On the T2-weighted image, this appears as mixed signal intensities within the cord (arrowed). (c) Post-mortem image of a dog that was euthanased secondary to deterioration of neurological signs. A durotomy has been performed. There is evidence of liquefactive necrosis of the cord parenchyma.
(c, Courtesy of S Behr, Willows Referral Service)



24.67 CT images. (a) Transverse and (b) dorsal multiplanar reconstruction images of a canine abdomen after contrast administration. A poorly defined soft tissue attenuating mass is present medial to the right kidney (arrowed). There is non-contrast-enhancing soft tissue attenuating material filling the retroperitoneum and dissecting between the retroperitoneal fat. Diagnosis: phaeochromocytoma and associated haemorrhage. This was a large dog and obtaining this level of detail by ultrasonography would have been very difficult.

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Chapter 25

Team approach to the critically ill patient – the role of the veterinary nurse

Emily Savino and Lila Sierra

Veterinary emergency services and critical care units provide advanced, specialized care and continuous 24-hour, 7-day a week monitoring to the most dynamic, fragile, critically ill patient population. A highly trained, multidisciplinary team of veterinary surgeons (veterinarians), nurses and support staff collaborate to provide intensive monitoring and state-of-the-art care. This team may consist of specialist clinicians and specialized veterinary nurses, and may also include experienced emergency veterinary surgeons, emergency and critical care (ECC) residents, interns, veterinary students and additional support staff. These clinical teams provide comprehensive patient care focused on optimizing patient outcomes and, ultimately, returning patients to their owners.

In this intense, demanding environment, it is essential that members of the critical care team work together as a cohesive unit to maximize successful patient outcomes. This chapter is focused on the team approach to the critically ill patient, emphasizing the role of the ECC nurse. Each of the topics discussed in this chapter: global monitoring and patient assessment; critical thinking; record keeping; and communication, collaboration and successful teamwork has its individual merits. However, when combined, they outline a team-centred approach to caring for the critically ill veterinary patient.

Global monitoring and patient assessment

Members of the critical care team must be able to rapidly assess and triage patients; treatment of the most critical cases must be prioritized over more stable cases. It is essential that all members of the intensive care unit (ICU) team, including veterinary nurses, are able to perform a physical examination quickly and competently. Of equal importance is the ability to interpret the resulting information and respond in an appropriate and efficient manner.

Critically ill patients are very dynamic; frequent, repeated physical assessments are necessary to evaluate a patient's response to treatment and detect subtle, but significant, changes in cardiovascular or respiratory status. Assessment of any one body system should not be interpreted independently – it is imperative that all of the information gathered during the physical assessment is compiled for an accurate global assessment of the patient's respiratory, cardiovascular, neurological and urinary systems.

Valuable information regarding the patient's cardiovascular and respiratory status can be obtained from advanced monitoring equipment; however, use of these monitors should not take precedence over performing a comprehensive physical examination. The nurse's initial physical examination should assess the major body systems that are vital for immediate survival: the cardiovascular, respiratory, central nervous and urinary systems.

Basic evaluation of the cardiovascular system

Basic cardiovascular assessment includes evaluation of mucous membrane colour, capillary refill time (CRT), heart rate and arterial pulse quality. Additional information regarding the patient's haemodynamics can be obtained from advanced monitoring equipment, including arterial blood pressure measurement, central venous pressure measurement and continuous electrocardiography.

Mucous membrane colour and capillary refill time

The oral mucous membrane colour is usually easiest to assess and the best site to use for CRT is the gingiva adjacent to the canine tooth (Figure 25.1), avoiding areas that are inflamed due to gingivitis. A normal animal should have pink mucous membranes. Variants of normal mucous membrane colour and CRT may give insight into the



25.1 The oral mucous membranes, showing the site where a capillary refill time should be performed.

patient's underlying condition. Pale, white, grey or muddy mucous membranes usually indicate poor perfusion or anaemia. Red or injected membranes may be associated with excitement, hyperthermia or systemic inflammatory response syndrome (SIRS) due to serious conditions such as sepsis or severe pancreatitis. Cyanotic mucous membranes indicate severe hypoxaemia. Icteric mucous membranes can result from increased red blood cell destruction or liver dysfunction. Other rare abnormalities of mucous membrane colour include the brown membranes seen with paracetamol (acetaminophen) poisoning in cats and the cherry red colour caused by carbon monoxide poisoning.

The CRT provides supplemental information that is particularly useful in the assessment of perfusion. A normal patient should have a CRT of 1–2 seconds. A CRT <1 second indicates a hyperdynamic state such as those observed in sepsis, SIRS and hyperthermia. A CRT >2 seconds suggests vasoconstriction and is commonly seen with hypovolaemia or other forms of shock

Heart rate and rhythm

The normal canine heart rate is approximately 70–120 bpm, with the degree of variation attributed to patient factors such as fitness. The normal feline heart rate range is 160–200 bpm in the veterinary environment, although it may be much lower in relaxed cats at home. Abnormal heart sounds, including murmurs, arrhythmias, gallop rhythms or muffled heart sounds, should be noted and monitored. Continuous electrocardiographic monitoring provides a non-invasive tool to observe and record abnormal heart rates or rhythms (Figure 25.2). Abnormalities noted on the electrocardiogram (ECG) should be recorded for review. Cardiac auscultation should be repeated several times daily to monitor for changes in heart rate or rhythm, or development of a new murmur.

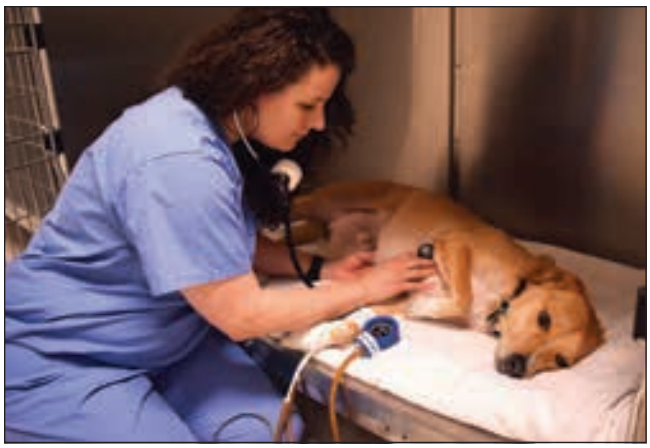


25.2 A multi-parameter monitor displaying a continuous ECG with a heart rate of 61 bpm.

Pulse quality

The pulse should be palpated while ausculting the heart. In a normal animal, a strong synchronous pulse should be felt for each heartbeat. Variations in pulse quality, a pulse that is asynchronous with a patient's heartbeat, or the presence of a pulse deficit indicates a cardiac arrhythmia. The continuous ECG can be utilized non-invasively to confirm and monitor an arrhythmia.

The femoral and dorsal pedal arteries are the most common locations for pulse palpation. The ability to palpate a pulse in each of these locations provides a rough estimate of systolic arterial blood pressure. The absence of a palpable dorsal pedal pulse may suggest a systolic blood pressure <80 mmHg. The absence of a palpable femoral pulse suggests a systolic blood pressure <50 mmHg. Additional considerations for describing pulse quality include pulse strength. For example, bounding pulses indicate a hyperdynamic state, with a large difference between the systolic and diastolic pressures, caused by a low diastolic pressure as a result of vasodilatation and hypovolaemia. Weak, thready pulses may be caused by severe hypovolaemia, decreased cardiac output and peripheral vasoconstriction. Cardiovascular system examination is commonly augmented by measurement of arterial blood pressure (Figure 25.3).



25.3 A veterinary nurse performing a cardiovascular examination by ausculting the heart. A blood pressure cuff can also be seen in place on the right forelimb.

Basic evaluation of the respiratory system

Members of the critical care team must remain acutely aware of the instability of dyspnoeic patients, which must be handled very carefully and subjected to as little stress as possible. These patients may benefit from a period of undisturbed rest in an oxygen cage set at a high oxygen concentration before a complete physical examination is attempted. It is sometimes best to perform the physical examination and treatments in stages, since excessive handling and manipulation of dyspnoeic patients may prove fatal.

Initial examination

Assessment of the respiratory system should include measurement of respiratory rate, evaluation of respiratory effort and auscultation of the upper respiratory tract and the lungs. A normal animal should have a respiratory rate of 15–30 breaths per minute and chest wall excursions that are visible but subtle. Abnormal respiratory rates or breathing patterns should be noted immediately and the reason for the abnormality must be identified.

Many dyspnoeic animals exhibit adaptive respiratory patterns or postural changes to decrease the work of breathing and prevent respiratory fatigue. Animals with upper airway obstruction or dynamic airway collapse often have a prolonged inspiratory phase with inspiratory stridor or stertor and a short expiratory phase. Patients with small airway disease, such as feline asthma, typi-cally have a longer expiratory than inspiratory phase, with increased respiratory effort on expiration. Patients with pleural space or interstitial lung disease such as pleural effusion, pneumothorax or pulmonary fibrosis may adopt a 'restrictive breathing pattern' resulting from de-creased ability to fully expand the lungs. Postural changes exhibited by animals in respiratory distress include adopting an orthopnoeic posture, which consists of standing rather than sitting, abduction of the elbows and stretching out the head and neck. Dyspnoeic cats may also exhibit a nasal flare. Open-mouth breathing in a cat is an overt sign of respiratory distress. A paradoxical respiratory pattern (lack of synchrony between excursions of the chest and abdomen) is often an indication that increased work of breathing is resulting in respiratory fatigue.

Auscultation

Examination of the respiratory system should include auscultation of the larynx, trachea and all lung fields bilaterally. Veterinary nurses working in emergency practice should develop auscultation skills. Some abnormal upper airway sounds can be heard without the aid of a stethoscope, including inspiratory stridor associated with laryngeal paralysis, inspiratory stertor characteristic of brachycephalic airway syndrome and the unmistakeable 'goose honk' cough of an animal with tracheal collapse.

Lung sounds in normal animals should auscult symmetrically when the same area is compared on both sides of the chest. Diminished lung sounds may be heard if there is lung consolidation, pneumothorax or pleural effusion. Pleural effusion causes lung sounds to be diminished ventrally, and pneumothorax results in dull lung sounds dorsally. Auscultation of crackles could indicate pulmonary oedema, pneumonia or pulmonary fibrosis. Assessment of respiratory rate and effort and lung auscultation should be repeated after aggressive fluid resuscitation and routinely evaluated several times throughout the day. Any significant changes in respiratory rate, effort or auscultation should be recorded and investigated.

Critically ill animals should have their oxygenation status evaluated frequently. The measurement of haemoglobin saturation (S_aO_2) using pulse oximetry offers a non-invasive measurement of a patient's ability to oxygenate. An S_aO_2 of <95% is indicative of hypoxaemia. Arterial blood gas analysis can also provide an assessment of oxygenation and ventilation. An arterial partial pressure of oxygen (P_aO_2) <80 mmHg signifies hypoxaemia. Severe hypoxaemia is indicated by S_aO_2 <90% or P_aO_2 <60 mmHg. In dyspnoeic animals, obtaining an arterial blood sample may prove too stressful, and clinical decisions can be made based on an accurate S_aO_2 reading.

Oxygen therapy

Supplemental oxygen should be provided for animals with any sign of respiratory distress or low S_aO_2. Oxygen therapy can be provided using an oxygen cage (Figure 25.4a), an oxygen mask (Figure 25.4b), short nasal prongs or an indwelling nasal cannula. Oxygen cages can provide a high concentration of oxygen and minimize additional stress for a dyspnoeic animal, and are particularly useful for initial stabilization of dyspnoeic cats. Animals in respiratory distress should be stabilized using 100% oxygen. Once the patient is more stable, oxygen concentration should be decreased to the minimal amount that will provide adequate systemic oxygenation. Administration of high concentrations of oxygen (fractional inspired oxygen concentration (F_iO_2) >60%) for prolonged periods of time (>12 hours) may cause oxygen toxicity.



25.4 (a) A patient in an oxygen cage. (b) A patient receiving oxygen supplementation by mask.

Basic evaluation of the neurological system

Critical illness is often associated with central nervous system depression; therefore, the neurological examination must take into consideration whether abnormalities in a patient's mental status are within the expectations for the patient's illness and any drugs it might have received. The basic neurological examination should include evaluation of the patient's level of consciousness (LOC), pupil size, pupillary light response, posture and reflexes. Ambulatory patients can also be observed for gait abnormalities. It may not be possible to complete a comprehensive neurological examination in certain cases, including those with extensive trauma or following recent administration of anxiolytics, opioids or anticonvulsants. Serial monitoring of neurological status is required to determine if a patient has responded to therapeutic intervention, has had no response to treatment or has progressively deteriorated despite treatment. Use of a standardized assessment such as the modified Glasgow Coma Scale is recommended.

The patient's mental status, responsiveness to stimuli and LOC should be evaluated frequently. Abnormalities in mental status include dull mentation, obtundation, stupor and coma. Neurological abnormalities may be the result of primary neurological disease or secondary to metabolic disease. For example, severe hypoglycaemia may cause dull mentation and/or seizures, and hepatic encephalopathy may result in an altered LOC, coma and seizure.

Patients with an abnormal LOC should be examined for a decreased or absent gag reflex by opening the mouth and palpating the pharynx. Decreased gag reflex places the animal at a high risk of aspiration. If the gag reflex is absent, either endotracheal intubation to protect the airway, or full or partial reversal of drugs, is indicated. Seizure activity requires immediate anticonvulsant therapy. Patients at risk for increased intracranial pressure must be closely monitored for signs of Cushing reflex (a combination of bradycardia with systemic hypertension; see Chapter 9). Supplemental oxygen should be administered in patients with a reduced LOC and oxygen saturation (S_aO_2) below 95%.

Basic evaluation of the urinary system

Basic evaluation of the urinary system includes monitoring urine production and urine specific gravity, and observation of any abnormalities in colour or odour of the urine. Additional information regarding the urinary system can be obtained using blood chemistry analysis (blood urea nitrogen (BUN), creatinine and potassium), urine dipsticks, and microscopic evaluation of the urine sediment. Measurement of urine output is of high importance in the critical care unit and is discussed below; analysis of the urine may also be important in some patients, but a detailed discussion of laboratory analysis is beyond the scope of this chapter.

Urine production

Urine production is an important indicator of renal function in critically ill patients. The frequency of monitoring and measuring urine output (UOP) may vary according to the individual patient. As a general rule, in catheterized patients UOP should be monitored every 4–6 hours and in some cases as frequently as every hour. UOP in well hydrated, well perfused patients that are not receiving excessive intravenous fluid therapy is typically 1–2 ml/kg/h.

UOP can be measured in several ways:

- Ambulatory canine patients can be walked and a rough quantitative estimate of their UOP can be recorded
- Ambulatory feline patients can use a litter tray and rough estimates of UOP are recorded; use of non-absorbent cat litter can facilitate a more accurate measurement
- Non-ambulatory patients may have indwelling urinary catheters. In this instance, the urine collection system can be emptied aseptically and the UOP quantified
- Alternatively, in the case of non-ambulatory patients without a urinary catheter, disposable absorbent pads (diapers) can be placed under the patient and the urine-soiled pads can be weighed. The weight of the dry pad/diaper is subtracted from the weight of the urine soaked pad/diaper to measure UOP (1 g = 1 ml of urine).

Decreased or increased UOP should be noted and investigated. Decreased UOP may result from primary acute kidney injury as well as pre-renal (i.e. hypovolaemia, hypoperfusion) and post-renal (i.e. urethral or ureteral obstruction, urinary tract rupture) causes. Confirmation of decreased UOP should be verified either by attempted manual palpation of the urinary bladder or by ultrasonography. In catheterized patients it is important to exclude mechanical problems with catheter collection systems as a possible cause of oliguria. Polyuria may result from renal disease, post-obstructive diuresis, diabetes mellitus, diabetes insipidus or an iatrogenic cause such as diuretic or steroid administration. Stranguria should be documented and monitored.

Gross examination and urine specific gravity

The gross appearance of the urine should be documented. Normal urine should be clear and pale yellow. Abnormalities such as a cloudy or turbid appearance and discolorations such as haematuria, haemoglobinuria or bilirubinuria should be noted and explored. Malodorous urine should also be investigated as it may indicate a urinary tract infection.

Urine specific gravity provides a quick indirect assessment of urine concentration. It helps differentiate pre-renal from post-renal azotaemia, and can support a diagnosis of renal insufficiency. Dehydrated animals should have concentrated urine (>1.035 in dogs, >1.050 in cats). Urine specific gravity values between 1.008 and 1.012 are considered to be isosthenuric. Hyposthenuria (specific gravity <1.008) may indicate renal insufficiency; however, other causes of dilute urine, including administration of intravenous fluids or diuretics, diabetes mellitus, diabetes insipidus, and hyperadrenocorticism, must be ruled out.

Critical thinking

The universal goal of the critical care team is to provide high-quality intensive care to patients with critical illnesses while maximizing favourable patient outcomes. To accomplish this goal, critical care providers engage in a process known as 'critical thinking'. Many definitions are used to describe critical thinking. For the purposes of this text, the concept is best defined by the American Association of Colleges of Nursing in the *Essentials of Baccalaureate Nursing*: 'Critical thinking underlies independent and interdependent decision making. Critical thinking includes questioning, analysis, synthesis, interpretation, inference, inductive and deductive reasoning, intuition, application and creativity.' (American Association of Colleges of Nursing, 1998). A simplified breakdown of the concepts involved in critical thinking is outlined in Figure 25.5.

Critical care providers tend to seriously ill patients with complex health problems. Positive patient outcomes increase when all members of the critical care team (including veterinary nurses) devote significant deliberation and clinical assessment to each patient. Decisions to proceed with a particular intervention are often based on theoretical knowledge, physical assessment of the patient, observation of patient trends and prior clinical experience.

Critical thinking requires excellent problem-solving skills. Critical care providers should have the ability to detect subtle but significant changes in a patient's status, predict potential complications, and intervene promptly to avoid undesired outcomes. The hallmark of successful critical thinkers in a clinical setting is the integration of a strong theoretical foundation with the ability to identify and prioritize problems requiring immediate attention, develop a patient care plan, evaluate the patient's response to treatment and reassess the patient to determine if further intervention is warranted. An integral part of the critical thinking process is to evaluate outcomes. Both desired

Concepts in critical thinking:
1. Identify the patient's primary problem/problems:
   - What are the patient's primary problems?
   - Are there any confirmed or differential diagnoses?
2. Collect additional information about the patient:
   - Perform a physical examination
   - Review patient data – look for trends
   - Apply theoretical knowledge: physiology, pathophysiology, pharmacology, etc.
3. Process information:
   - Interpret and analyse the data – identify normal *versus* abnormal values
   - Recognize specific trends or changes in the patient's condition. Determine if any of the changes are interrelated
   - Draw upon past experiences – has this situation been encountered before?
   - Predict an expected outcome.
4. Identify the problems and issues:
   - Combine all of the information to identify the problem to be addressed.
5. Determine a patient care plan:
   - How are the problems being addressed?
   - What are the expected results?
   - What is the expected timeframe to observe results?
6. Act: carry out the intervention.
7. Evaluate the outcome:
   - Has the patient improved?
8. Review:
   - Reassess the situation and evaluate the outcome
   - Is further intervention indicated?
   - If so, is a different intervention or the same intervention indicated?

25.5 An approach to critical thinking.
(Adapted from Levett-Jones *et al.*, 2010)

and undesired outcomes provide an opportunity for reflection and learning.

It is important to consider the application of critical thinking as it relates to the critical care team as a whole. Critical care teams usually include clinicians and nurses with different levels of clinical experience and expertise. Those with limited clinical experience may be more likely to miss subtle but significant cues, or may reassess patients or re-evaluate data less frequently than experienced practitioners. Warning signs often precede adverse events; however, a subtle decline in a patient's status may go unnoticed. In contrast, expert clinicians and nurses are able to make assessments based on knowledge and prior experience and successfully predict the most likely immediate outcome. The ability to predict potential complications prompts creation of an action plan and preparation for rapid intervention if necessary.

The relationship between critical thinking and the team approach to critical care should not be overlooked. Through collaboration and mentoring, expert clinicians and nurses can help less experienced team members develop their clinical reasoning skills, systematically think through problems and prioritize patients in need of immediate care. Senior team members often demonstrate advanced problem-solving skills, proactive case management and evolved decision-making skills. Expert practitioners can assist less experienced staff members to be prepared for potential patient complications by sharing their previous clinical experiences.

Record keeping

A patient's record is a written extension of the verbal communication between veterinary surgeons, nurses, technicians, assistants and aides. In a busy hospital setting, it can seem next to impossible to track patient changes, activities, procedures and test results. Keeping a precise, detailed patient record can prove to be equally as important as the care provided.

Many different team members (and even departments in a larger hospital) may provide care for one patient over the course of a day. Having thorough documentation should provide a seamless account of those events. Thus, each team member will not only be able to understand how to pick up where the last person left off, but can easily continue to monitor trends and detect changes in the patient's status.

Maintaining an accurate patient record is a painstaking process and should be a shared responsibility amongst the entire team. Any caregiver who has interacted with a patient on any level should enter it into the record. On busy days, it may seem as though documentation is an inefficient use of precious time, but those are the times when having recorded details in fine print can prove their worth. Later review of a patient's medical record assists in presentation of complete, detailed rounds at shift change, and may also trigger recall of other important facts inadvertently left out of the record.

From a legal standpoint, any medical record is subject to scrutiny. If an executed action (treatment, medication, owner communication) is not documented, it may be interpreted as not having been performed at all. The maxim 'if it's not written down, it didn't happen' is worth remembering.

The standard of medical recording may also be viewed as an indirect reflection of the standard of care. No matter how well a patient was treated, a poor medical record may not reflect the care that has been provided. Figures 25.6 and 25.7 provide guidance on important aspects of medical record keeping.

- Write legibly in dark ink (blue or black), never in pencil.
- Make sure any supplemental pages added to the record are labelled with:
  - Patient identification
  - Date
  - Page numbers.
- Document all observations, treatments and communications in a clear, detailed and consecutive order:
  - Adding a time to each entry gives the reader a frame of reference
  - Record your findings in the way that you sensed them (sight, hearing, touch, smell).
- Incorrect entries should be corrected by drawing a single line through/over the entry, then signing and dating the record. The modified statement may be added next to it.
  - Do not 'scratch out' or use 'white out'. Legally, the medical record is considered evidence and errors must remain legible.
- Do not use slang, jargon or offensive statements. Keep it professional and use proper medical terminology.

25.6 Important principles of medical record keeping.

- Notes should include a complete description of your examination, care provided, status of the patient, communications with the primary clinician, and any future course of action for continued care.
- Enter events immediately after they have happened, as important details will be easier to recall at the time. Chaotic periods in a hospital are unpredictable and unavoidable, so it may be helpful to jot down a few key notes/words, and return to the record as soon as things settle down that day to complete a 'late entry'.
- Provide detailed explanations to keep everyone informed of your thought process at the time of your notation: Examples:
  - 'Patient has recently vomited and was unable to take scheduled oral medications. Will NPO at this time and consult with clinician'
  - 'Patient sleeping comfortably. Will not disturb at this time and continue treatments when he/she wakes up'
  - 'Patient's blood glucose trending low. Will discuss findings with clinician and consider rechecking another value in 1 hour'.

25.7 How to write nursing notes in a medical record.

The type of record format used will depend on the practice and the department. Medical records may have an electronic or paper format. For example, referral practices that encompass different specialties (i.e. ECC, surgery, internal medicine) may desire a format with charts and progress notes for documenting serial measurement of vitals, fluid therapy, bloodwork results, and an area to write down assessments (Figures 25.8 and 25.9). A general practice might find that too detailed and opt for a different structure. Electronic medical records are making their way into veterinary medicine and can be constructed around the particular needs of each practice.

Veterinary Hospital of the University of Pennsylvania
Intensive Care Unit Treatment Orders

	Problem list	
Date		
Clinician: Student:	Code: DNR ☐ Basic life support ☐ Advanced life support ☐	
Body weight (kg)	Blood type:	Previously transfused? Y/N/U
Infectious disease? Y/N/Suspect =	Diet:	Additional notes:

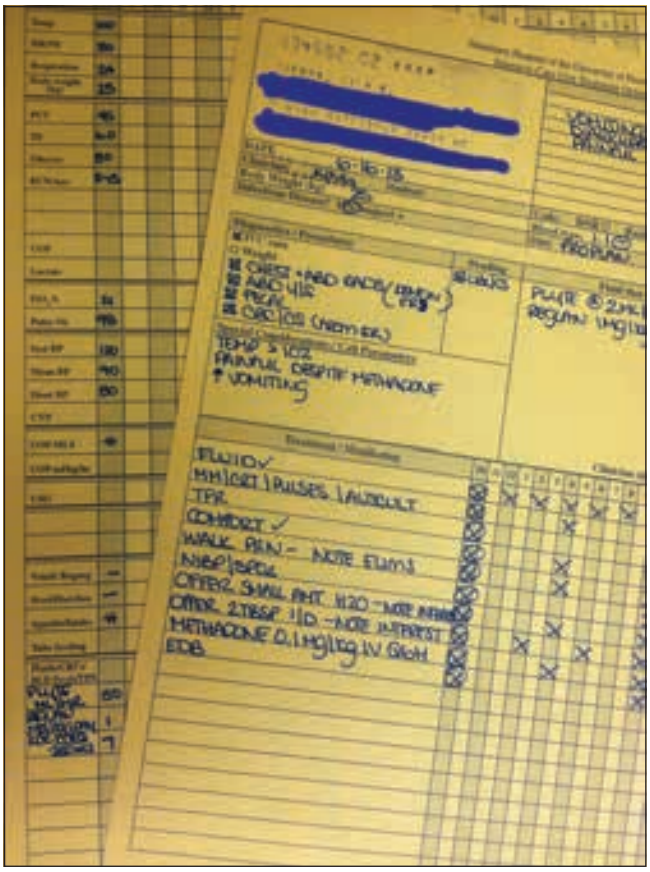
Diagnostics/procedures	Pending	Fluid therapy and continuous infusions
☐ IVC care ☐ Weight		
Special considerations/call parameters		Clinician signature.....

Treatment/monitoring	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9

25.8 An example of a blank ICU treatment sheet (front and back). (continues) ▶

Time	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7
Temp																								
HR/PR																								
Respiration																								
Body weight (kg)																								
PCV																								
TS																								
Glucose																								
BUN/Azo																								
COP																								
Lactate																								
FiO_2%																								
Pulse ox																								
Syst BP																								
Mean BP																								
Diast BP																								
CVP																								
UOP mls																								
UOP ml/kg/hr																								
USG																								
Vomit/regurg																								
Stool/diarrhoea																								
Appetite/intake																								
Tube feeding																								
Fluids/CRIs/bld prods/TPN																								

25.8 (continued) An example of a blank ICU treatment sheet (front and back).



25.9 An example of a completed treatment sheet showing (right) the transcription of a patient's orders and (left) documentation of vitals.

Communication, collaboration and successful teamwork

During hospitalization in a 24-hour, 7-day a week critical care unit, a patient may have been examined and treated by several different staff members. In order to make sense of the information coming from this assortment of individuals, it is crucial to have an organized system of teamwork, communication and collaboration.

The best healthcare facilities are recognized not only for the new and innovative technologies they offer but also for their effective structure of teamwork and multidisciplinary (or interdisciplinary) approach to patient care. Fostering an effectively functioning, cohesive team results in job satisfaction, decreased response time to patient needs, and practice efficiency.

Strong team leaders play an essential role in cultivating a cohesive team by providing direction, feedback and resources. Wearing multiple 'hats', they play mentor, cheerleader and, at times, mediator. There should be opportunities for the group to establish standards and expectations of integrity, to discuss visions and values, and to design performance guidelines.

One of the most fundamental ingredients of a successful team is mutual trust and respect, particularly between clinicians and nurses, and vice versa. Development of trust and respect naturally requires a 'probationary' period when new team members are introduced so that individuals can become acquainted with one another's skill sets, educational backgrounds and personalities. It is important to encourage a continuous flow of dialogue within the group. Routine communication and information sharing increases awareness of everyone's knowledge and abilities. Dialogue does not have to be solely about patient care, but also should involve exchange of ideas and concepts that promote career development for staff members. For example, new clinicians and nurses can learn to perfect their assessment, clinical or practical skills with help from the experience and knowledge of more senior staff members. This exercise not only establishes rapport and strengthens the 'trust bond', but leads to ongoing improvements in decision making (Figure 25.10).

Smooth teamwork requires clear, concise goals for patient care. In critical care, goals may change at a moment's notice in response to changes in a patient's condition, so it is equally important that goals are adaptable and changes are communicated regularly amongst the staff. Fragmented objectives or a lapse in updates will create confusion and inconsistency, and could result in medical errors.

Tasks should be delegated on an individual level. Encouraging staff to feel a sense of ownership of their assignments provides freedom to use individual 'styles' of skill sets while keeping in mind the contribution to the team and the overall objective.

While there may be an overall sense of togetherness, respect, and even affection between members of a workplace team, it is not uncommon for conflicts to arise from time to time. It is important to recognize the conflict and address it immediately, as allowing conflict to fester will create tension for the team. Working through difficulties and approaching resolutions with dialogue and a sense of diplomacy may produce constructive ideas to avoid future disagreements.

Team accomplishments and individual successes should always be acknowledged. In this field, where the daily stresses of ECC can take their toll on wellbeing and morale, it is extremely important to recognize dedication and hard work. Rewards and recognition are powerful, positive reinforcement tools. Rewarding staff for their successes will promote similar behaviours in the future and provide them with the necessary motivation to sustain high performance.

Routine assessment of teamwork and its effect on patient outcomes is an excellent barometer of overall performance. Each patient is unique and poses its own set of challenging circumstances. Taking a look at how your team responded to specific challenges highlights what worked, what did not work, and the effectiveness of the



25.10 Discussions about a case provide an opportunity to bond with other members of the clinical team.

team structure and leadership. Taking into consideration all of those factors, the team can fine-tune its protocols and continue to evolve (Figure 25.11).

- Mutual trust and respect.
- Open dialogue/routine communication/information sharing.
- Clear goals, roles and assignments.
- Balance of individual participation.
- Conflict management/resolution.
- Enabling, positive environment.
- Examination of outcomes and making improvements.

25.11 Ingredients of a successful team.

Acknowledgement

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BSAVA Manual of Canine and Feline

Emergency and Critical Care

Third edition

Edited by Lesley G. King and Amanda Boag



Emergency care is one of the most important areas of veterinary medicine. Building on the success of the previous editions, the international editors and authors have reviewed and updated the Manual to reflect the continued growth in knowledge and understanding in this crucial area.

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